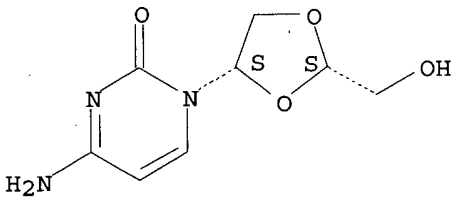
```
=> fil hcap
FILE 'HCAPLUS' ENTERED AT 12:54:04 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 16 Mar 2005  VOL 142 ISS 12
FILE LAST UPDATED: 15 Mar 2005  (20050315/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> fil reg
FILE 'REGISTRY' ENTERED AT 12:54:07 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   15 MAR 2005  HIGHEST RN 845699-17-4
DICTIONARY FILE UPDATES:  15 MAR 2005  HIGHEST RN 845699-17-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> => d que l60
L56 (         1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  US2003-729387/APPS
L57             SEL  PLU=ON  L56 1- RN :       6 TERMS
L58           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  L57
L59      127705 SEA FILE=REGISTRY ABB=ON  PLU=ON  ?DIOXOLAN?/CNS
L60           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L58 AND L59


=> d ide l60 1-2

L60  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   145918-75-8  REGISTRY
```

CN **2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(1H)-Pyrimidinone, 4-amino-1-[2-(hydroxymethyl)-1,3-dioxolan-4-yl]-, (2S-cis)-**
OTHER NAMES:
CN (-)-BCH 204
CN (-)-OccC
CN BCH 4556
CN L-OddC
CN SPD 758
CN Troxacitabine
CN Troxatyl
FS STEREOSEARCH
MF C8 H11 N3 O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMINFORMRX, CIN, EMBASE, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry. Rotation (-).



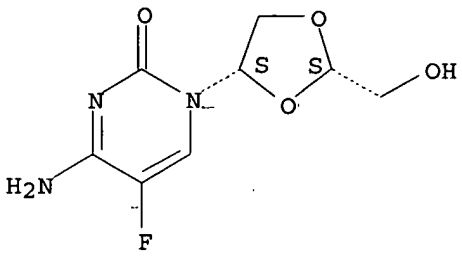
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

78 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
80 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L60 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN **145397-26-8** REGISTRY
CN **2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[2-(hydroxymethyl)-1,3-dioxolan-4-yl]-, (2S-cis)-**
FS STEREOSEARCH
MF C8 H10 F N3 O4
SR CA
LC STN Files: CA, CAPLUS, CHEMINFORMRX, MEDLINE, PROUSDDR, SYNTHLINE,

TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d que l3
L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN

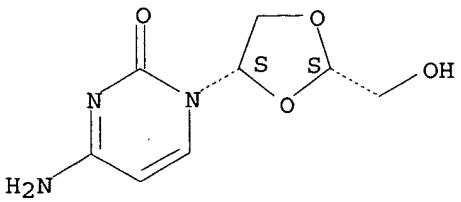
=> d ide l3 1-2

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 790208-79-6 REGISTRY
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate, mixt. with 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-2(1H)-pyrimidinone (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H31 N7 O . C8 H11 N3 O4 . C H4 O3 S
CI MXS
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

CM 1

CRN 145918-75-8
CMF C8 H11 N3 O4

Absolute stereochemistry. Rotation (-).

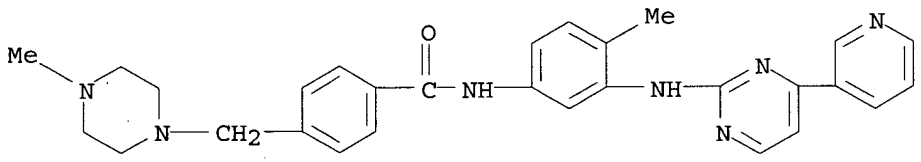


CM 2

CRN 220127-57-1
CMF C29 H31 N7 O . C H4 O3 S

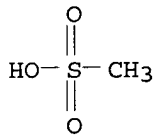
CM 3

CRN 152459-95-5
CMF C29 H31 N7 O



CM 4

CRN 75-75-2
CMF C H4 O3 S



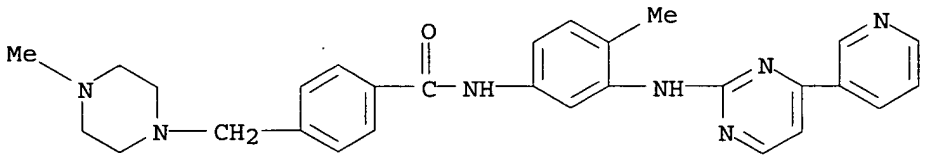
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN **220127-57-1** REGISTRY
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CGP 57148B
CN Gleevac
CN Gleevec
CN Glivec
CN Imatinib mesilate
CN Imatinib mesylate
CN STI 571

MF C29 H31 N7 O . C H4 O3 S
CI COM
SR CA
LC STN Files: ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, EMBASE, HSDB*, IMSPATENTS, IMSRESEARCH, MRCK*, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)

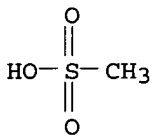
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



857 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
863 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> => fil hcap
FILE 'HCAPLUS' ENTERED AT 13:21:22 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 16 Mar 2005 VOL 142 ISS 12
FILE LAST UPDATED: 15 Mar 2005 (20050315/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> fil medlin
FILE 'MEDLINE' ENTERED AT 13:21:25 ON 16 MAR 2005

FILE LAST UPDATED: 15 MAR 2005 (20050315/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP
RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> fil biosis
FILE 'BIOSIS' ENTERED AT 13:21:28 ON 16 MAR 2005

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 9 March 2005 (20050309/ED)

FILE RELOADED: 19 October 2003.

=> fil embase
FILE 'EMBASE' ENTERED AT 13:21:30 ON 16 MAR 2005

FILE COVERS 1974 TO 10 Mar 2005 (20050310/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil drugu
FILE 'DRUGU' ENTERED AT 13:21:33 ON 16 MAR 2005

FILE LAST UPDATED: 10 MAR 2005 <20050310/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

>>> A RECENT REVIEW OF PSYCHIATRIC DISEASE KEYWORDS USED IN DERWENT DRUG FILE HAS PROMPTED A REVISION BASED ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH EDITION).
FOR FURTHER DETAILS:
http://thomsonderwent.com/derwenthome/support/userguides/lit_guide

=> fil wpix
FILE 'WPIX' ENTERED AT 13:21:37 ON 16 MAR 2005

FILE LAST UPDATED: 11 MAR 2005 <20050311/UP>
MOST RECENT DERWENT UPDATE: 200517 <200517/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-revision/
FOR DETAILS. <<<

=> fil pascal
FILE 'PASCAL' ENTERED AT 13:21:41 ON 16 MAR 2005

FILE LAST UPDATED: 14 MAR 2005 <20050314/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
IN THE BASIC INDEX (/BI) FIELD <<<

=> fil jicst
FILE 'JICST-EPLUS' ENTERED AT 13:21:45 ON 16 MAR 2005
COPYRIGHT (C) 2005 Japan Science and Technology Agency (JST)

FILE COVERS 1985 TO 14 MAR 2005 (20050314/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

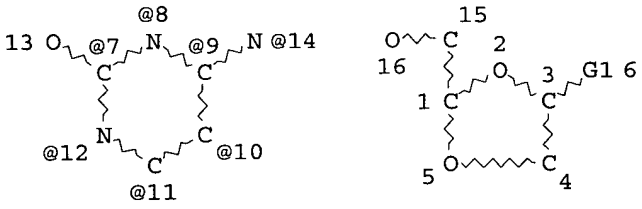
=> fil scisearch
FILE 'SCISEARCH' ENTERED AT 13:21:49 ON 16 MAR 2005
Copyright (c) 2005 The Thomson Corporation

FILE COVERS 1974 TO 10 Mar 2005 (20050310/ED)

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:21:50 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 11, 2005 (20050311/UP).

=> d que l16
L4 STR

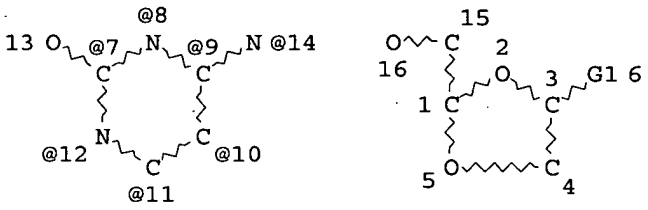


VAR G1=7/8/9/14/10/11/12
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

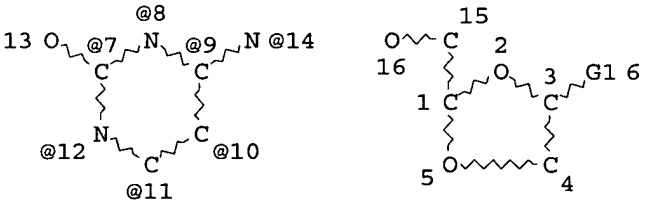
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L5 (452) SEA FILE=REGISTRY SSS FUL L4
L6 (2) SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN
L7 (116) SEA FILE=HCAPLUS ABB=ON PLU=ON L5
L8 (863) SEA FILE=HCAPLUS ABB=ON PLU=ON L6
L9 (11) SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND L8

```
L10             QUE  ABB=ON  PLU=ON  (?TYROSIN?(2A)?KINAS?) (3A) (?INHIBI
                T? OR ?RUPT? OR ?BLOCK? OR ?MODERAT? OR ?MODULAT?)
L11             QUE  ABB=ON  PLU=ON  ?IMATINIB? (2A) ?MESYL?
L12             QUE  ABB=ON  PLU=ON  STI(1W)571
L13 (         8)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND ((L10 OR L11 OR L12))
L14             QUE  ABB=ON  PLU=ON  ?TYROSIN?(2A)?KINAS?
L15 (         5)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L14
L16          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L13 OR L15


=> d que l33
L1              STR
```




```
VAR G1=7/8/9/14/10/11/12
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L2          452 SEA FILE=REGISTRY SSS FUL L1
L11             QUE  ABB=ON  PLU=ON  ?IMATINIB? (2A) ?MESYL?
L12             QUE  ABB=ON  PLU=ON  STI(1W)571
L14             QUE  ABB=ON  PLU=ON  ?TYROSIN?(2A)?KINAS?
L19             STR
```




```
VAR G1=7/8/9/14/10/11/12
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L20 (       452)SEA FILE=REGISTRY SSS FUL L19
L21 (         2)SEA FILE=REGISTRY ABB=ON  PLU=ON  220127-57-1/RN,CRN
L22             SEL  PLU=ON  L20 1- CHEM :     474 TERMS
```

```
L23 (         86)SEA FILE=MEDLINE ABB=ON  PLU=ON  L22
L24               SEL  PLU=ON  L21 1- CHEM :        9 TERMS
L25 (       1112)SEA FILE=MEDLINE ABB=ON  PLU=ON  L24
L26            9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L23 AND L25
L30               SEL  PLU=ON  L2 1- CHEM :      474 TERMS
L31           86 SEA FILE=MEDLINE ABB=ON  PLU=ON  L30
L32            9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L31 AND (L11 OR L12 OR L14)
L33           10 SEA FILE=MEDLINE ABB=ON  PLU=ON  L32 OR L26


=> d que nos l40
L1                STR
L2            452 SEA FILE=REGISTRY SSS FUL L1
L3              2 SEA FILE=REGISTRY ABB=ON  PLU=ON  220127-57-1/RN,CRN
L11               QUE  ABB=ON  PLU=ON  ?IMATINIB? (2A) ?MESYL?
L12               QUE  ABB=ON  PLU=ON  STI(1W)571
L14               QUE  ABB=ON  PLU=ON  ?TYROSIN?(2A)?KINAS?
L34               SEL  PLU=ON  L2 1- CHEM :      474 TERMS
L35           125 SEA FILE=EMBASE ABB=ON  PLU=ON  L34
L36               SEL  PLU=ON  L3 1- CHEM :        9 TERMS
L37          3491 SEA FILE=EMBASE ABB=ON  PLU=ON  L36
L38            24 SEA FILE=EMBASE ABB=ON  PLU=ON  L35 AND L37
L39            20 SEA FILE=EMBASE ABB=ON  PLU=ON  L35 AND (L14 OR L11 OR L12)
L40            27 SEA FILE=EMBASE ABB=ON  PLU=ON  L38 OR L39


=> d que nos l48
L1                STR
L2            452 SEA FILE=REGISTRY SSS FUL L1
L3              2 SEA FILE=REGISTRY ABB=ON  PLU=ON  220127-57-1/RN,CRN
L12               QUE  ABB=ON  PLU=ON  STI(1W)571
L14               QUE  ABB=ON  PLU=ON  ?TYROSIN?(2A)?KINAS?
L41               QUE  ABB=ON  PLU=ON  ?IMATINIB?
L42               SEL  PLU=ON  L2 1- CHEM :      474 TERMS
L43           98 SEA FILE=BIOSIS ABB=ON  PLU=ON  L42
L44               SEL  PLU=ON  L3 1- CHEM :        9 TERMS
L45         1470 SEA FILE=BIOSIS ABB=ON  PLU=ON  L44
L46            5 SEA FILE=BIOSIS ABB=ON  PLU=ON  L43 AND L45
L47            4 SEA FILE=BIOSIS ABB=ON  PLU=ON  L43 AND (L41 OR L14 OR L12)
L48            5 SEA FILE=BIOSIS ABB=ON  PLU=ON  L46 OR L47


=> d que nos l55
L1                STR
L2            452 SEA FILE=REGISTRY SSS FUL L1
L3              2 SEA FILE=REGISTRY ABB=ON  PLU=ON  220127-57-1/RN,CRN
L12               QUE  ABB=ON  PLU=ON  STI(1W)571
L14               QUE  ABB=ON  PLU=ON  ?TYROSIN?(2A)?KINAS?
L41               QUE  ABB=ON  PLU=ON  ?IMATINIB?
L49               SEL  PLU=ON  L2 1- CHEM :      474 TERMS
L50           104 SEA FILE=DRUGU ABB=ON  PLU=ON  L49
L51               SEL  PLU=ON  L3 1- CHEM :        9 TERMS
L52          1077 SEA FILE=DRUGU ABB=ON  PLU=ON  L51
L53            7 SEA FILE=DRUGU ABB=ON  PLU=ON  L50 AND L52
L54            8 SEA FILE=DRUGU ABB=ON  PLU=ON  L50 AND (L14 OR L41 OR L12)
L55            9 SEA FILE=DRUGU ABB=ON  PLU=ON  L53 OR L54


=> d que l78
L64           12 SEA FILE=WPIX ABB=ON  PLU=ON  ((?TROXACITABIN?/BIX OR ?TROXATYL
```

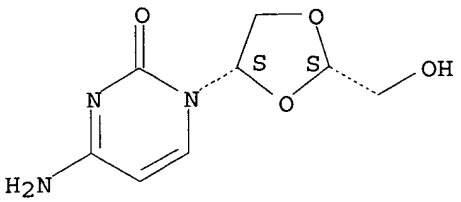
```
                ?/BIX OR (SPD/BIX(1W)758/BIX) OR OCCC/BIX OR (BCH/BIX(1W)(204/B
                IX OR 4556/BIX)) OR (?DIOXALAN?/BIX(1W)C/BIX)))
L65          48 SEA FILE=WPIX ABB=ON  PLU=ON  (((CGP/BIX(1W)57148B/BIX) OR
                ?GLEEVAC?/BIX OR ?GLEEVEC?/BIX OR ?GLIVEC?/BIX))
L66        2131 SEA FILE=WPIX ABB=ON  PLU=ON  (?TYROSIN?/BIX(2A)?KINAS?/BIX)
L67          77 SEA FILE=WPIX ABB=ON  PLU=ON  (?IMATINIB?/BIX)
L68          16 SEA FILE=WPIX ABB=ON  PLU=ON  (STI/BIX(1W)571/BIX)
L69           6 SEA FILE=WPIX ABB=ON  PLU=ON  L64 AND (L65 OR L66 OR L67 OR
                L68)
L70       13221 SEA FILE=WPIX ABB=ON  PLU=ON  (B14-S09 OR C14-S09 OR B12-C09
                OR C12-C09)/MC
L71           2 SEA FILE=WPIX ABB=ON  PLU=ON  L64 AND L70
L72           2 SEA FILE=WPIX ABB=ON  PLU=ON  L65 AND L70
L73          11 SEA FILE=WPIX ABB=ON  PLU=ON  L67 AND L70
L74          11 SEA FILE=WPIX ABB=ON  PLU=ON  (L71 OR L72 OR L73)
L75       18409 SEA FILE=WPIX ABB=ON  PLU=ON  A61P035?/IPC
L76       57371 SEA FILE=WPIX ABB=ON  PLU=ON  (B14-H? OR C14-H?)/MC
L77          11 SEA FILE=WPIX ABB=ON  PLU=ON  L74 AND (L75 OR L76)
L78          15 SEA FILE=WPIX ABB=ON  PLU=ON  L69 OR L77


=> d his l82

     (FILE 'PASCAL, JICST-EPLUS, SCISEARCH' ENTERED AT 13:11:56 ON 16 MAR 2005)
L82           6 DUP REM L81 (4 DUPLICATES REMOVED)

=> d que l82
L12              QUE  ABB=ON  PLU=ON  STI(1W)571
L14              QUE  ABB=ON  PLU=ON  ?TYROSIN?(2A)?KINAS?
L41              QUE  ABB=ON  PLU=ON  ?IMATINIB?
L62              QUE  ABB=ON  PLU=ON  (?TROXACITABIN? OR ?TROXATYL? OR (SP
                 D(1W)758) OR OCCC OR (BCH(1W)(204 OR 4556)) OR (?DIOXALAN
                 ?(1W)C))
L63              QUE  ABB=ON  PLU=ON  ((CGP(1W)57148B) OR ?GLEEVAC? OR ?GL
                 EEVEC? OR ?GLIVEC?)
L79         134 SEA L62
L80       65582 SEA (L63 OR L12 OR L41 OR L14)
L81          10 SEA L79 AND L80
L82           6 DUP REM L81 (4 DUPLICATES REMOVED)


=> dup rem l16 l33 l40 l48 l55 l78 l82
FILE 'HCAPLUS' ENTERED AT 13:23:20 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 13:23:20 ON 16 MAR 2005

FILE 'EMBASE' ENTERED AT 13:23:20 ON 16 MAR 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'BIOSIS' ENTERED AT 13:23:20 ON 16 MAR 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'DRUGU' ENTERED AT 13:23:20 ON 16 MAR 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'WPIX' ENTERED AT 13:23:20 ON 16 MAR 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION
```

FILE 'PASCAL' ENTERED AT 13:23:20 ON 16 MAR 2005

FILE 'SCISEARCH' ENTERED AT 13:23:20 ON 16 MAR 2005

PROCESSING COMPLETED FOR L16
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L40
PROCESSING COMPLETED FOR L48
PROCESSING COMPLETED FOR L55
PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L82
L89 54 DUP REM L16 L33 L40 L48 L55 L78 L82 (30 DUPLICATES REMOVED)
ANSWERS '1-12' FROM FILE HCAPLUS
ANSWERS '13-18' FROM FILE MEDLINE
ANSWERS '19-37' FROM FILE EMBASE
ANSWER '38' FROM FILE BIOSIS
ANSWERS '39-45' FROM FILE DRUGU
ANSWERS '46-54' FROM FILE WPIX

```
=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:23:46 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 11, 2005 (20050311/UP).

=> d ibib ed abs fhitstr hitind
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
CONTINUE? (Y)/N:y


L89  ANSWER 1 OF 54  HCAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:1036851  HCAPLUS
DOCUMENT NUMBER:          142:696
TITLE:                    Synergistic treatment of cancer using immunomers in
                          conjunction with chemotherapeutic agents
INVENTOR(S):              Kandimalla, Ekambar R.; Agrawal, Sudhir; Wang, Daqin
PATENT ASSIGNEE(S):       Hybridon, Inc., USA
SOURCE:                   PCT Int. Appl., 106 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004103301         A2    20041202    WO 2004-US15313         20040514
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     US 2005009773         A1    20050113    US 2004-846167          20040514
PRIORITY APPLN. INFO.:                       US 2003-471247P     P   20030516
OTHER SOURCE(S):          MARPAT 142:696
ED   Entered STN:  03 Dec 2004
AB   The invention discloses the therapeutic use of immunostimulatory
     oligonucleotides and/or immunomers in combination with chemotherapeutic
     agents to provide a synergistic therapeutic effect.
IT   145918-75-8, BCH-4556
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (immunostimulatory oligonucleotide and/or immunomer combination with
        chemotherapeutic agent for synergistic cancer treatment)
RN   145918-75-8  HCAPLUS
CN   2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-
     yl]- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.  Rotation (-).
```



IC ICM A61K
CC 1-6 (Pharmacology)
IT 50-07-7, Mitomycin C 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa 53-19-0, Mitotane 55-86-7, Mechlorethamine hydrochloride 55-98-1, Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 69-74-9, Cytarabine hydrochloride 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 143-67-9, Vinblastine sulfate 145-63-1, Suramin 147-94-4, DepoCyte 148-82-3, Melphalan 154-93-8, Carmustine 305-03-3, Chlorambucil 320-67-2, Azacitidine 366-70-1, Procarbazine hydrochloride 459-86-9, Mitoguazone 645-05-6, Hexamethylmelamine 3094-09-5, Furtulon 3778-73-2 4291-63-8, Leustatin 4342-03-4, Dacarbazine 9015-68-3, Asparaginase 11056-06-7, Bleomycin 11096-26-7, Erythropoietin 13010-20-3D, Nitrosourea, derivs. 13010-47-4, Lomustine 13311-84-7, Flutamide 13909-09-6, Semustine 14769-73-4, Levamisole 15663-27-1, Cisplatin 16595-80-5, Ergamisol 18378-89-7, Plicamycin 18883-66-4, Streptozocin 19764-02-4, Fragilin 19767-45-4, Mesna 23214-92-8, Evacet 23541-50-6, Daunorubicin hydrochloride 25316-40-9, Adriamycin 29767-20-2, Vumon 33069-62-4, Yewtaxan 33419-42-0 38270-90-5, Metastron 38819-10-2D, Guaninearabinoside, prodrug derivative 39325-01-4, Picibanil 41575-94-4, Paraplatin 51264-14-3, Amsacrine 52205-73-9, Estramustine phosphate sodium 53910-25-1, 2'Deoxycoformycin 54965-24-1, Tamoxifen citrate 56124-62-0, Valrubicin 56420-45-2, Pharmarubicin 59917-39-4, Vindesine sulfate 59989-18-3, Eniluracil 65271-80-9, Novantrone 66849-34-1, D 4809 70476-82-3, Mitoxantrone hydrochloride 74381-53-6, Leuprolide acetate 74578-38-4, Uft 75607-67-9, Fludara 83150-76-9, Octreotide 85622-93-1, Temodal 90409-78-2, Polifeprosan 91421-43-1, 9-Aminocamptothecin 95058-81-4, Gemcitabine 97682-44-5, Camptosar 100286-90-6, Campto 102409-92-7, FK 317 106400-81-1, LY 264618 112522-64-2, CI-994 112887-68-0, Tomudex 114977-28-5, Taxotere 119876-18-5D, non-sugar-containing derivs. 120685-11-2, PKC412 121584-18-7, Valspodar 122111-03-9, Gemzar 123948-87-8, Topotecan 129298-91-5, TNP-470 129580-63-8, BMS 182751 130370-60-4, Batimastat 141907-41-7 **145918-75-8**, BCH-4556 146426-40-6, HMR 1275 150399-23-8, LY231514 151823-14-2, CS-682 153537-73-6, ZD 9331 154039-60-8, TA 2516 154361-50-9, Xeloda 159776-69-9, LU.103793 159997-94-1, Incel 162706-37-8, LU 79553 165668-41-7, E7070 169799-04-6, MMI270 169869-90-3, DX8951 f 174722-31-7, Rituxan 179545-77-8, BAY 12-9566 180288-69-1, Herceptin 181630-15-9, ZD 0473 183012-14-8, YM 116 183319-69-9, CP 358774 184046-91-1 184475-35-2, ZD1839 190454-58-1, VX 853 192329-42-3, AG3340 209164-46-5, CDP 845 **220127-57-1**, Gleevec 259188-38-0, D2163 289499-45-2, PD183805 386211-12-7, AG 3433 386211-13-8, ZD 0101 386211-20-7, ISI 641 386211-21-8, ODN 698 386211-47-8, Lemonal DP 2202 386211-48-9, CP 609754 799292-77-6, Glamolec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunostimulatory oligonucleotide and/or immunomer combination with chemotherapeutic agent for synergistic cancer treatment)

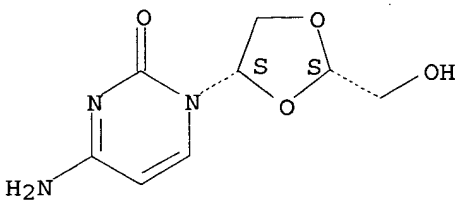
=> d ibib ed abs fhitstr hitind 2-12
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
CONTINUE? (Y)/N:y

L89 ANSWER 2 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:965080 HCAPLUS
DOCUMENT NUMBER: 141:388665
TITLE: Method for infusion administration of troxacitabine for the treatment of cancer
INVENTOR(S): Jolivet, Jacques; Gourdeau, Henriette
PATENT ASSIGNEE(S): Shire Biochem Inc., Can.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096239	A1	20041111	WO 2004-CA446	20040324
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004248915	A1	20041209	US 2004-806336	20040323
PRIORITY APPLN. INFO.:			US 2003-465228P P	20030425

ED Entered STN: 12 Nov 2004
AB In the treatment of cancer, troxacitabine or a pharmaceutically acceptable salt can be effectively administered to a host having a tumor by continuous infusion for a period of at least 72 h, wherein the amount is sufficient to provide tumor reduction
IT **145918-75-8**, Troxacitabine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine infusion for treatment of cancer)
RN 145918-75-8 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-704
ICS A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 63
IT **145918-75-8**, Troxacitabine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine infusion for treatment of cancer)
IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine 51-75-2, Mechlorethamine 53-03-2, Prednisone 55-98-1, Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 127-07-1, Hydroxyurea 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, 6-Thioguanine 154-93-8, Carmustine 302-79-4, Retinoic acid 305-03-3, Chlorambucil 671-16-9, Procarbazine 865-21-4, Vinblastine 1404-00-8, Mitomycin 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4342-03-4, Dacarbazine 9014-42-0, Thrombopoietin 9015-68-3, Asparaginase 11056-06-7, Bleomycin 11096-26-7, Epoetin 13010-47-4, Lomustine 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 33419-42-0, Etoposide 53910-25-1, Pentostatin 58957-92-9, Idarubicin 62683-29-8, Colony-stimulating factor 65271-80-9, Mitoxantrone 83869-56-1, GM-CSF 95058-81-4, Gemcitabine 121181-53-1, Filgrastim 121584-18-7, PSC 833 123774-72-1, Sargramostim 123948-87-8, Topotecan 143011-72-7, G-CSF 174722-31-7, Rituxan **220127-57-1**, Gleevec 220578-59-6, CMA-676 **790208-65-0**
790208-66-1 790208-67-2 790208-68-3
790208-69-4 790208-70-7 790208-71-8
790208-72-9 790208-73-0 790208-74-1
790208-75-2 790208-76-3 790208-77-4
790208-78-5 790208-79-6 790208-80-9
790208-81-0 790208-82-1 790208-83-2
790208-84-3 790208-85-4 790208-86-5
790208-87-6 790208-88-7 790208-89-8
790208-90-1 790208-91-2 790208-92-3
790208-93-4 790208-94-5 790208-95-6
790208-96-7 790208-97-8 790208-98-9
790208-99-0 790209-00-6 790209-01-7
790209-02-8 790209-03-9 790209-04-0
790209-05-1 790209-06-2 790209-07-3
790209-08-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine infusion for treatment of cancer, and use with other agents)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

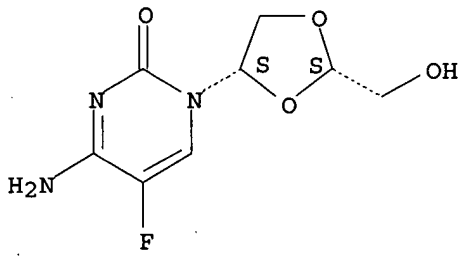
L89 ANSWER 3 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:513542 HCAPLUS
DOCUMENT NUMBER: 141:47311

TITLE: Pharmaceutical combinations and methods using dioxolanyl cytosine derivatives and dioxolanyl 5-fluorocytosine derivatives for the treatment of leukemia
INVENTOR(S): Giles, Francis J.; Verstovsek, Srdan
PATENT ASSIGNEE(S): Shire Biochem Inc., Can.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052369	A1	20040624	WO 2003-CA1909	20031208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004192652	A1	20040930	US 2003-729387	20031208
PRIORITY APPLN. INFO.:			US 2002-431196P P	20021206

OTHER SOURCE(S): MARPAT 141:47311
ED Entered STN: 25 Jun 2004
AB The invention provides a pharmaceutical combination useful for the treatment of leukemia comprising at least one cytosine or 5-fluorocytosine derivative and a Bcr-Abl **tyrosine kinase inhibitor**, as well as a method of treating a patient having leukemia comprising at least one cytosine or 5-fluorocytosine derivative and a Bcr-Abl **tyrosine kinase inhibitor.**
IT **145397-26-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dioxolanyl cytosine derivs. and dioxolanyl 5-fluorocytosine derivs. for treatment of leukemia)
RN 145397-26-8 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IC ICM A61K031-506
ICS A61K031-513; A61P035-00; A61P035-02

CC 1-6 (Pharmacology)
ST cytosine dioxolanyl deriv Bcr Abl **tyrosine kinase inhibitor** leukemia; fluorocytosine dioxolanyl deriv Bcr Abl **tyrosine kinase inhibitor** leukemia
IT 138238-67-2, Bcr-Abl **tyrosine kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dioxolanyl cytosine derivs. and dioxolanyl 5-fluorocytosine derivs. for treatment of leukemia)
IT 71-30-7D, Cytosine, dioxolanyl derivs. 2022-85-7D, 5-Fluorocytosine, dioxolanyl derivs. **145397-26-8 145918-75-8 220127-57-1, Imatinib mesylate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dioxolanyl cytosine derivs. and dioxolanyl 5-fluorocytosine derivs. for treatment of leukemia)

L89 ANSWER 4 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:453016 HCAPLUS
DOCUMENT NUMBER: 141:1227
TITLE: Combination cancer therapy with a glutathione S-transferase (GST)-activated anticancer compound and another anticancer therapy
INVENTOR(S): Xu, Hua; Brown, Gail L.; Schow, Steven R.; Keck, James G.
PATENT ASSIGNEE(S): Telik, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045593	A2	20040603	WO 2003-US36209	20031114
WO 2004045593	A3	20040812		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004138140	A1	20040715	US 2003-714593	20031114
PRIORITY APPLN. INFO.:			US 2002-426983P	P 20021115

OTHER SOURCE(S): MARPAT 141:1227
ED Entered STN: 04 Jun 2004
AB The invention discloses a method for combination cancer therapy in a mammal, especially a human, by administering a therapeutically effective amount of a GST-activated anticancer compound and a therapeutically ED of another anticancer therapy. Also disclosed are pharmaceutical compns., products, and kits for the method, as well as the use of a GST-activated anticancer compound in the manufacture of a medicament for the method. The invention further discloses a method for potentiating an anticancer therapy in a mammal, especially a human, comprising administering a therapeutically effective

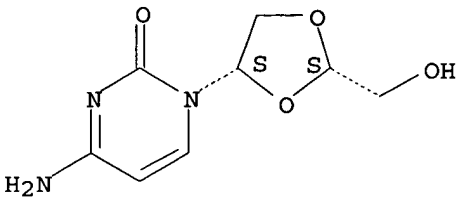
amount of a GST-activated anticancer compound to the mammal being treated with the anticancer therapy. Further disclosed is the use of a GST-activated anticancer compound in the manufacture of a medicament for the method. The GST-activated anticancer compound is preferably a compound of US Patent Number 5,556,942, and more preferably TLK286, especially as the hydrochloride salt.

IT **145918-75-8**, Troxacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy with GST-activated anticancer compound and another anticancer therapy)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-00

CC 1-6 (Pharmacology)
Section cross-reference(s): 63

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 50-91-9, Floxuridine 51-21-8, Fluorouracil 51-48-9, Levothyroxine, biological studies 51-75-2, Mechlorethamine 52-24-4, Thiotepa 53-03-2, Prednisone 53-19-0, Mitotane 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 58-05-9, Leucovorin 59-05-2, Methotrexate 66-75-1, Uramustine 71-58-9, Medroxyprogesteroneacetate 76-43-7, Fluoxymesterone 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 145-63-1, Suramin 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine 298-81-7, Methoxsalen 302-79-4, trans-Retinoic acid 305-03-3, Chlorambucil 320-67-2, Azacitidine 566-48-3, Formestane 595-33-5, Megestrol acetate 645-05-6, Altretamine 671-16-9, Procarbazine 801-52-5, Porfiromycin 865-21-4, Vinblastine 958-09-8D, chloro derivs. 968-93-4, Testolactone 1327-53-3, Arsenic trioxide 1404-00-8, Mitomycin 1605-68-1, Taxane 2098-66-0, Cyproterone 2998-57-4, Estramustine 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4342-03-4, Dacarbazine 5300-03-8, 9-cis-Retinoic acid 6893-02-3, Liothyronine 7440-06-4D, Platinum, compds. 9015-68-3, L-Asparaginase 9015-68-3D, L-Asparaginase, PEG conjugates 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13010-47-4, Lomustine 13311-84-7, Flutamide 13494-90-1, Galliumnitrate 14769-73-4, Levamisole 15663-27-1, Cisplatin 18378-89-7, Mithramycin 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 25322-68-3D, PEG, L-asparaginase conjugates 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 51264-14-3, Amsacrine 52128-35-5, Trimetrexate 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 56124-62-0, Valrubicin 56420-45-2, Epirubicin 57773-63-4, Triptorelin 57982-77-1, Buserelin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 63612-50-0, Nilutamide 65271-80-9, Mitoxantrone 65646-68-6, N-(4-Hydroxyphenyl)retinamide 65807-02-5, Goserelin 71486-22-1, Vinorelbine 80576-83-6, Edatrexate 83150-76-9, Octreotide

84449-90-1, Raloxifene 85622-93-1, Temozolomide 87806-31-3, Photofrin Porfimer sodium 89778-26-7, Toremifene 90357-06-5, Bicalutamide 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 106685-40-9, Adapalene 107868-30-4, Exemestane 110942-02-4, Aldesleukin 112809-51-5, Letrozole 112887-68-0, Raltitrexed 114977-28-5, Docetaxel 120511-73-1, Anastrozole 123318-82-1, Clofarabine 123948-87-8, Topotecan 129453-61-8, Fulvestrant 129580-63-8, Satraplatin 137281-23-3, Pemetrexed **145918-75-8**, Troxacitabine 145941-26-0, Oprelvekin 153559-49-0, Bexarotene 154361-50-9, Capecitabine 158382-37-7 173146-27-5, Denileukin diftitox 174722-31-7, Rituximab 179324-69-7, Bortezomib 180288-69-1, Trastuzumab 181630-15-9 183319-69-9 184475-35-2, Gefitinib 192391-48-3 194413-58-6, Semaxanib 205923-56-4, Cetuximab 206181-63-7 216503-57-0, Alemtuzumab 216974-75-3, Bevacizumab **220127-57-1**, **Imatinib mesylate** 220578-59-6, Gemtuzumab Ozogamicin 439943-59-6, Canglustratide hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination cancer therapy with GST-activated anticancer compound and another anticancer therapy)

IT 80449-02-1, Protein **tyrosine kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; combination cancer therapy with GST-activated anticancer compound and another anticancer therapy)

L89 ANSWER 5 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2004:334928 HCAPLUS
DOCUMENT NUMBER: 140:399534
TITLE: Troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukaemia: preclinical evaluation
AUTHOR(S): Orsolic, Nada; Giles, Francis J.; Gourdeau, Henriette; Golemovic, Mirna; Beran, Miloslav; Cortes, Jorge; Freireich, Emil J.; Kantarjian, Hagop; Verstovsek, Srdan
CORPORATE SOURCE: Department of Leukemia, M.D. Anderson Cancer Center, The University of Texas, Houston, TX, USA
SOURCE: British Journal of Haematology (2004), 124(6), 727-738
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Apr 2004
AB The in vitro and in vivo activity of a deoxycytidine analog, troxacitabine, alone or in combination with **imatinib mesylate** (IM), was evaluated against human chronic myeloid leukemia (CML) cell lines both sensitive (KBM5 and KBM7) and resistant (KBM5-R and KBM7-R) to IM. These cell lines differ in their sensitivity to IM but all showed similar sensitivity to treatment with troxacitabine (IC50 = 0.5-1 μmol/l). Combined treatment with troxacitabine and IM revealed additive or synergistic effects. Greater apoptotic response was seen with, combined treatment than with either agent alone in KBM7-R cells. In clonogenic assays, troxacitabine showed activity against mononuclear cells from CML patients (IC50 = 0.01 μmol/l) with either IM-sensitive or resistant disease. In vivo efficacy studies were carried out in severe combined immunodeficient mice bearing KBM5 or KBM5-R cells. Troxacitabine was administered i.p. daily for 5 d starting on day 20, at doses of 5, 10, 20, or 25 mg/kg. IM was administered i.p. twice a day for 10 d at a dose of 50 mg/kg starting on day 25. In this setting of late stage disease, troxacitabine led to a significant increase in life span,

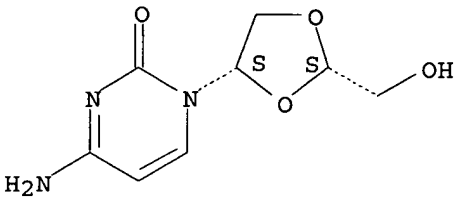
while IM did not. When IM was combined with troxacitabine at 10 and 25 mg/kg in the KBM5 xenograft model, a further increase in life span was observed and some mice achieved long-term survival. These data indicate that the combination of troxacitabine and IM has significant preclin. activity in advanced CML and that clin. evaluation of this combination is warranted.

IT **145918-75-8**, Troxatyl
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-6 (Pharmacology)

ST troxacitabine **imatinib mesylate** antitumor resistance chronic myeloid leukemia

IT Drug resistance
(antitumor; troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT Leukemia
(chronic myelocytic; troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT Antitumor agents
(resistance to; troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT Antitumor agents
Human
(troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT **145918-75-8**, Troxatyl **220127-57-1**, Gleevec
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 6 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2004:868814 HCAPLUS

DOCUMENT NUMBER: 142:168637

TITLE: Nucleoside analogs and antimetabolite therapies for myelodysplastic syndrome

AUTHOR(S): Foss, Francine M.

CORPORATE SOURCE: Department of Hematology-Oncology and Experimental Therapeutics, Bone Marrow Transplant Program, Tufts New England Medical Center, Boston, MA, 02111, USA

SOURCE: Best Practice & Research, Clinical Haematology (2004),

17(4), 573-584
CODEN: BPRCA5
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 20 Oct 2004

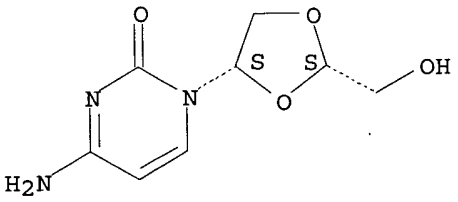
AB A review. Myelodysplastic syndrome (MDS) is a heterogeneous group of clonal hematopoietic disorders. Therapeutic interventions for MDS other than allogeneic bone marrow transplantation have been palliative. Because most of the patients are elderly and may not be candidates for ablative transplant conditioning regimens, treatment has focused on supportive care. Recently, several novel biol. and chemotherapeutic agents have demonstrated activity in MDS and are being incorporated into the treatment paradigm. These agents are based on specific mechanisms aimed at angiogenesis in the bone marrow, secretion of growth factors and/or their receptors, and modulators in their intracellular pathways. Several agents are in the initial stages of clin. trial, including anti-vascular endothelial growth factor, bevacizumab, receptor **tyrosine kinase inhibitors**, farnesyl transferase **inhibitors**, protein kinase C inhibitors, matrix metalloproteinase inhibitors and other agents such as thalidomide and arsenic trioxide. Novel chemotherapeutic agents include topoisomerase inhibitors such as topotecan and rubitecan, and deoxyadenosine analogs such as troxacitabine, tezacitabine, and clofarabine. Prognostic factors predicting response in MDS patients treated with intensive chemotherapy have been identified and include younger age and favorable cytogenetics.

IT **145918-75-8**, Troxacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(deoxyadenosine analogs such as troxacitabine for patients with myelodysplastic syndrome are discussed)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-0 (Pharmacology)

IT **145918-75-8**, Troxacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(deoxyadenosine analogs such as troxacitabine for patients with myelodysplastic syndrome are discussed)

IT 340830-03-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor **tyrosine kinase inhibitor** is in initial stages of clin. trial for myelodysplastic syndrome in human)

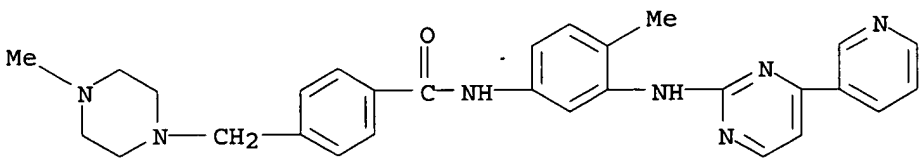
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 7 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 2004:599447 HCAPLUS
DOCUMENT NUMBER: 142:85532
TITLE: Biology of chronic myeloid leukemia and possible therapeutic approaches to imatinib-resistant disease
AUTHOR(S): Yoshida, Chikashi; Melo, Junia V.
CORPORATE SOURCE: Department of Haematology, Hammersmith Hospital, Imperial College London, London, UK
SOURCE: International Journal of Hematology (2004), 79(5), 420-433
CODEN: IJHEEY; ISSN: 0925-5710
PUBLISHER: Carden Jennings Publishing
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 27 Jul 2004
AB A review. Chronic myeloid leukemia (CML) is a stem cell disorder caused by a constitutively activated **tyrosine kinase**, the Bcr-Abl oncoprotein. An **inhibitor** of this **tyrosine kinase**, **imatinib mesylate**, is rapidly becoming the first-line therapy for CML. However, the development of resistance to this drug is a frequent setback, particularly in patients in advanced phases of the disease. Several mechanisms of resistance have been described, the most frequent of which are amplification and/or mutations of the BCR-ABL gene. To overcome resistance, several approaches have been studied in vitro and in vivo. They include dose escalation of imatinib, combination of imatinib with chemotherapeutic drugs, alternative Bcr-Abl inhibitors, inhibitors of kinases downstream of Bcr-Abl, farnesyl and geranylgeranyl transferase inhibitors, histone deacetylase, proteasome and cyclin-dependent kinase inhibitors, arsenic trioxide, hypomethylating agents, troxacitabine, targeting Bcr-Abl mRNA, and immunomodulatory strategies. It is important to understand that these approaches differ in efficiency, which is often dependent on the mechanisms of resistance. Further investigations into the mol. mechanisms of disease and how to specifically target the abnormal processes will guide the design of new treatment modalities in future clin. trials.
IT **220127-57-1**, **Imatinib mesylate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dose escalation, combination with chemotherapeutic drugs, alternative Bcr-Abl, kinase, transferase inhibitors and targeting Bcr-Abl mRNA and immunomodulatory strategies are possible therapeutic approaches to imatinib-resistant CML)
RN 220127-57-1 HCAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

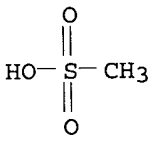
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



CC 1-0 (Pharmacology)
IT **220127-57-1, Imatinib mesylate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dose escalation, combination with chemotherapeutic drugs, alternative Bcr-Abl, kinase, transferase inhibitors and targeting Bcr-Abl mRNA and immunomodulatory strategies are possible therapeutic approaches to imatinib-resistant CML)
IT **145918-75-8**, Troxacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine is one of possible therapeutic approach to imatinib-resistant chronic myeloid leukemia disease both in vitro and in vivo)
REFERENCE COUNT: 164 THERE ARE 164 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 8 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 2003:737931 HCAPLUS
DOCUMENT NUMBER: 139:255332
TITLE: Method for selecting antitumor drug sensitivity-determining factors and method for predicting antitumor drug sensitivity using the selected factors
INVENTOR(S): Aoki, Yuko; Hasegawa, Kiyoshi; Ishii, Nobuya; Mori, Kazushige
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076660	A1	20030918	WO 2002-JP2354	20020313

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,

GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2478640	AA	20030918	CA 2002-2478640	20020313
EP 1483401	A1	20041208	EP 2002-705127	20020313

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: WO 2002-JP2354 W 20020313

ED Entered STN: 19 Sep 2003

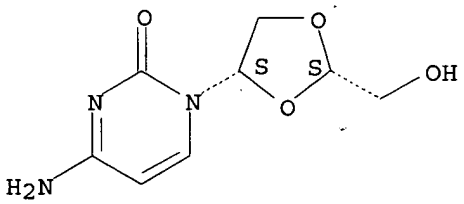
AB Based on drug sensitivity data and extensive gene expression data, a model was constructed by multivariate anal. with the partial least squares method type 1. Further, the model was optimized using modeling power and genetic algorithm. Thereby, the degree of contribution of the resp. genes to drug sensitivity was determined to select genes with a high degree of contribution. In addition, the levels of gene expression in specimens were analyzed, and then the drug sensitivity was predicted based on the model. The predicted values agreed well with those drug sensitivity values determined exptl. The drug sensitivity-predicting method provided by the present invention enables assessment of the effectiveness of a drug prior to administration using small quantities of specimens associated with diseases such as cancer. Since this enables the selection of the most suitable drug for each patient, the present invention is very useful in improving a patient's quality of life (QOL).

IT **145918-75-8**, Troxacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for selecting antitumor drug sensitivity-determining factors and predicting antitumor drug sensitivity using the selected factors)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM C12Q001-68
ICS G06K009-62; G06F017-17

CC 1-6 (Pharmacology)
Section cross-reference(s): 2

IT 51-21-8, 5-FU 66-22-8, 2,4(1H,3H)-Pyrimidinedione, biological studies 147-94-4, Ara-C 2207-75-2, Potassium oxonate 2353-33-5, Decitabine 3094-09-5, Furtulon 4291-63-8, Cladribine 7689-03-4, Camptothecin 10540-29-1, Tamoxifen 15663-27-1, Cisplatin 17902-23-7, Tegafur 20830-81-3, Daunomycin 25316-40-9, Adriamycin 33069-62-4, Taxol 41575-94-4, Carboplatin 53714-56-0, Leuprorelin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 61422-45-5, Carmofur 75607-67-9 82640-04-8, LY156758 90357-06-5, ZD 176334 91421-42-0, 9-Nitrocamptothecin 91421-43-1, 9-Aminocamptothecin 100286-90-6, CPT-11 103766-25-2, 5-Chloro-2,4-dihydroxypyridine 105149-00-6, TZP4238 107868-30-4, FCE24304 110417-88-4, Dolastatin 10 112809-51-5, CGS 20267 114977-28-5, Taxotere 115767-74-3, TAT59 119804-96-5, DMDC 120511-73-1, ZD 1033 120685-11-2, CGP41251 123884-00-4, Dolastatin 15 123948-87-8, Topotecan 126723-15-7, Dolastatin 14 **145918-75-8**,

Troxacitabine 149606-27-9, TZT 1027 154361-50-9, Xeloda 159776-69-9, Cemadotin 160237-25-2, BMS 184476 169869-90-3, DX-8951f 171179-06-9, PD 158780 172481-83-3, BMS 188797 172903-00-3, BBR 3464 182133-25-1, LY353381 182167-03-9, EM800 183319-69-9, CP 358774 184475-35-2, ZD 1839 186348-23-2, IDN 5109 189453-10-9, Epothilone D 192185-68-5, R115777 193275-84-2, SCH66336 195987-41-8, BMS 214662 204005-46-9, SU5416 212142-18-2, PTK787 212631-79-3, CI1040 219989-84-1, BMS 247550 **220127-57-1**, **STI-571** 220997-97-7, BN-80915 252916-29-3, SU6668 253863-00-2, L778123 284461-73-0, BAY 439006 437755-78-7, GW 2016 443913-73-3, ZD6474 601517-74-2, GW 2286
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for selecting antitumor drug sensitivity-determining factors and predicting antitumor drug sensitivity using the selected factors)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 9 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 2003:202456 HCAPLUS
DOCUMENT NUMBER: 138:231710
TITLE: Treatment of chronic myelogenous leukemia, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents
INVENTOR(S): Robin, Jean-Pierre; Mahon, Francois-Xavier; Maisonneuve, Herve; Maloisel, Frederick; Blanchard, Julie
PATENT ASSIGNEE(S): Oncopharm Corporation, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020252	A2	20030313	WO 2002-IB3992	20020905
WO 2003020252	A3	20030619		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1443933	A2	20040811	EP 2002-772653	20020905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004019036	A1	20040129	US 2003-397267	20030327
PRIORITY APPLN. INFO.:			US 2001-316967P	P 20010905
			WO 2002-IB3992	W 20020905

ED Entered STN: 14 Mar 2003
AB The present invention concerns a method of treating chronic myelogenous leukemia (CML), a related myeloproliferative disorder or a Ph-pos. acute lymphocytic leukemia in a subject animal, comprising: (a) selecting or identifying an animal suffering from chronic myelogenous leukemia or a related myeloproliferative disorder and showing resistance or intolerance

to treatment with STI571; and (b) administering to the animal homoharringtonine. In a preferred embodiment, the animal is a human being. Significant sensitivity to homoharringtonine was observed in progenitors from patients relapsing on STI571 therapy both before and after relapse,, strongly implying that in CML blast crisis cells refractory to STI751 there is no significant cross-resistance to homoharringtonine.

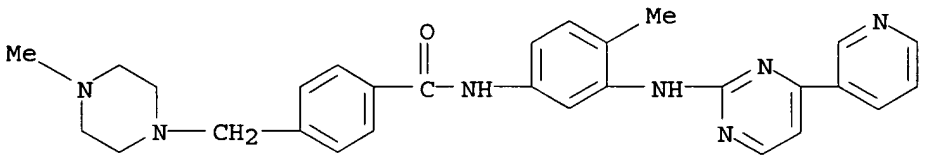
IT **220127-57-1**, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic myelogenous leukemia, resistant or intolerant to STI571, treatment with homoharringtonine alone or combined with other agents)

RN 220127-57-1 HCAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

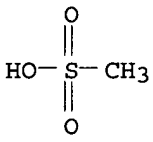
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



IC ICM A61K031-00
CC 1-6 (Pharmacology)

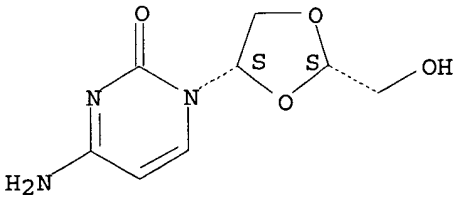
IT 26833-87-4, Homoharringtonine **220127-57-1**, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic myelogenous leukemia, resistant or intolerant to STI571, treatment with homoharringtonine alone or combined with other agents)

IT 147-94-4, Cytarabine 2353-33-5, Decitabine 25322-68-3D, Peg, conjugates with interferons **145918-75-8**, Troxacitabine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic myelogenous leukemia, resistant or intolerant to STI571, treatment with homoharringtonine alone or combined with other agents)

L89 ANSWER 10 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 12
ACCESSION NUMBER: 2003:621850 HCAPLUS

DOCUMENT NUMBER: 140:228562
TITLE: Phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase
AUTHOR(S): Giles, Francis J.; Feldman, Eric J.; Roboz, Gail J.; Larson, Richard A.; Mamus, Steven W.; Cortes, Jorge E.; Verstovsek, Srdan; Faderl, Stefan; Talpaz, Moshe; Beran, Miloslav; Albitar, Maher; O'Brien, Susan M.; Kantarjian, Hagop M.
CORPORATE SOURCE: M.D. Anderson Cancer Center, Department of Leukemia, University of Texas, Houston, TX, 77030, USA
SOURCE: Leukemia Research (2003), 27(12), 1091-1096
CODEN: LEREDD; ISSN: 0145-2126
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Aug 2003
AB A phase II study of troxacitabine, a non-natural dioxolane nucleoside L-enantiomer, was conducted in patients with chronic myelogenous leukemia in blastic phase (CML-BP). Patients were untreated for BP, or treated with **imatinib mesylate** (IM) as sole prior therapy for BP. Troxacitabine was given as an i.v. infusion over 30 min daily for 5 days at a dose of 8.0 mg/m2 per day. Thirty-one patients, 29 (93%) of whom had failed prior IM therapy, received 51 courses of therapy. Grade 3 or 4 toxicities included stomatitis (4%), hand-foot syndrome (18%), and skin rash (12%). Four patients (13%) responded. Troxacitabine-based combinations merit study in IM-resistant CML.
IT **145918-75-8**, Troxacitabine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)
RN 145918-75-8 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-6 (Pharmacology)
ST antitumor troxacitabine **imatinib mesylate** resistant chronic myelogenous leukemia; dioxolane nucleoside analog antitumor **imatinib mesylate** resistant myelogenous leukemia
IT Drug resistance
(antitumor; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)
IT Leukemia
(chronic myelocytic; phase II study of troxacitabine, a novel dioxolane

nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT Antitumor agents
(chronic myelogenous leukemia; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT Human
(phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate** -resistant chronic myelogenous leukemia in blastic phase)

IT Antitumor agents
(resistance to; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT **145918-75-8**, Troxacitabine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate** -resistant chronic myelogenous leukemia in blastic phase)

IT **220127-57-1**, **Imatinib mesylate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(resistance; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 11 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:80347 HCAPLUS
DOCUMENT NUMBER: 140:122775
TITLE: Treatment of chronic myelogenous leukemia, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents
INVENTOR(S): Robin, Jean-pierre; Mahon, Francois-xavier; Maisonneuve, Herve; Maloisel, Frederick; Blanchard, Julie
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of Appl. No. PCT/IB02/03992.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004019036	A1	20040129	US 2003-397267	20030327
WO 2003020252	A2	20030313	WO 2002-IB3992	20020905
WO 2003020252	A3	20030619		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-316967P P 20010905
WO 2002-IB3992 A2 20020905

ED Entered STN: 01 Feb 2004

AB The invention concerns a method of treating chronic myelogenous leukemia, a related myeloproliferative disorder or a Ph-pos. acute lymphocytic leukemia in a subject animal, comprising: (a) selecting or identifying an animal suffering from chronic myelogenous leukemia or a related myeloproliferative disorder and showing resistance or intolerance to treatment with STI571; and (b) administering to the animal homoharringtonine. In a preferred embodiment, the animal is a human.

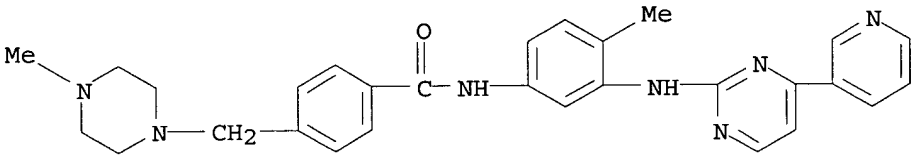
IT **220127-57-1**, STI571
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of CML, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents)

RN 220127-57-1 HCAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

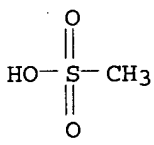
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



IC ICM A61K031-55
NCL 514214030
CC 1-6 (Pharmacology)
Section cross-reference(s): 15, 63
IT 147-94-4, Cytarabine 26833-87-4, Homoharringtonine **220127-57-1**
, STI571

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of CML, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents)

IT 2353-33-5, Decitabine **145918-75-8**, Troxacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of CML, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents)

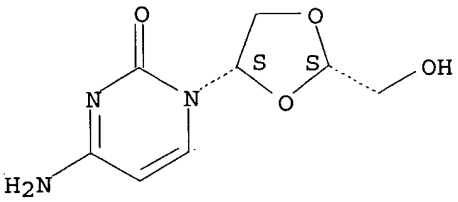
L89 ANSWER 12 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:356264 HCAPLUS
DOCUMENT NUMBER: 138:348696
TITLE: Pharmaceutical compositions for the treatment of leukemia comprising dioxolane nucleosides analogs
INVENTOR(S): Jolivet, Jacques; Giles, Francis J.; Kantarjian, Hagop
PATENT ASSIGNEE(S): Shire Biochem Inc., Can.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037344	A1	20030508	WO 2002-CA1687	20021104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20031253O5	A1	20030703	US 2002-286960	20021104
US 6645972	B2	20031111		
EP 1441733	A1	20040804	EP 2002-771956	20021104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-330891P P 20011102
WO 2002-CA1687 W 20021104

OTHER SOURCE(S): MARPAT 138:348696
ED Entered STN: 09 May 2003
AB The present invention provides a novel method for treating leukemia in a host that has been previously treated with a Bcr-Abl **tyrosine kinase inhibitor** comprising administering to the host a therapeutically effective amount of a dioxolane nucleoside analog.
IT **145918-75-8**, Troxatyl
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dioxolane nucleoside analog for treatment of leukemia)
RN 145918-75-8 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-506
ICS A61P035-02
CC 1-6 (Pharmacology)
IT 138238-67-2, Bcr-Abl **tyrosine kinase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dioxolane nucleoside analog for treatment of leukemia)
IT **145918-75-8**, Troxatyl **220127-57-1**, **Imatinib mesylate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dioxolane nucleoside analog for treatment of leukemia)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib ed ab hitind 13
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' - CONTINUE? (Y)/N:y

L89 ANSWER 13 OF 54 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2004043980 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14745859
TITLE: New agents in acute myeloid leukemia and other myeloid disorders.
AUTHOR: Ravandi Farhad; Kantarjian Hagop; Giles Francis; Cortes Jorge
CORPORATE SOURCE: Department of Leukemia, The University of Texas M D Anderson Cancer Center, Houston, Texas 77030, USA.. fravandi@mdanderson.org
SOURCE: Cancer, (2004 Feb 1) 100 (3) 441-54. Ref: 140
Journal code: 0374236. ISSN: 0008-543X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040128
Last Updated on STN: 20040220
Entered Medline: 20040219
ED Entered STN: 20040128
Last Updated on STN: 20040220
Entered Medline: 20040219
AB Over the past several decades, improvements in chemotherapeutic agents and supportive care have resulted in significant progress in treating patients with acute myeloid leukemia (AML). More recently, advances in understanding the biology of AML have resulted in the identification of new therapeutic targets. The success of all-trans-retinoic acid in acute

promyelocytic leukemia and of **imatinib mesylate** in chronic myeloid leukemia have demonstrated that targeted therapy may be more effective and less toxic when well defined targets are available. At the same time, understanding mechanisms of drug resistance and means to overcome them has led to modification of some of the existing cytotoxic agents. Rational design and conduct of clinical trials is necessary to ensure that the full potential of these new agents is realized.
Copyright 2003 American Cancer Society.

CT Check Tags: Comparative Study; Female; Male
*Antineoplastic Agents: TU, therapeutic use
Cyclosporine: TU, therapeutic use
*Cytosine: AA, analogs & derivatives
Cytosine: TU, therapeutic use
*Deoxycytidine: AA, analogs & derivatives
Deoxycytidine: TU, therapeutic use
Dioxolanes: TU, therapeutic use
Humans
*Immunosuppressive Agents: TU, therapeutic use
Immunotherapy: MT, methods
Leukemia, Myelocytic, Acute: DI, diagnosis
*Leukemia, Myelocytic, Acute: DT, drug therapy
Leukemia, Myelocytic, Acute: MO, mortality
Prognosis
Randomized Controlled Trials
Risk Assessment
Severity of Illness Index
Survival Analysis
Treatment Outcome

RN 103882-84-4 (gemcitabine); **145918-75-8 (troxacitabine)**; 59865-13-3 (Cyclosporine); 71-30-7 (Cytosine); 951-77-9 (Deoxycytidine)

CN 0 (Antineoplastic Agents); 0 (Dioxolanes); 0 (Immunosuppressive Agents)

=> d ibib ed ab hitind 14-45
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' - CONTINUE? (Y)/N:y

L89 ANSWER 14 OF 54 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2004098430 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14988742
TITLE: Gateways to clinical trials.
AUTHOR: Bayes M; Rabasseda X; Prous J R
CORPORATE SOURCE: Prous Science, PO Box 540, 08080 Barcelona, Spain.. mbayes@prous.com
SOURCE: Methods and findings in experimental and clinical pharmacology, (2004 Jan-Feb) 26 (1) 53-84. Ref: 200 Journal code: 7909595. ISSN: 0379-0355.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20040510
Entered Medline: 20040507

ED Entered STN: 20040302
Last Updated on STN: 20040510

Entered Medline: 20040507

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity, the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: Abetimus sodium, Ad5-FGF4, adeno-Interferon gamma, AE-941, AERx, alemtuzumab, alicaforsen sodium, almotriptan, alpharadin, anakinra, anatumomab mafenatox, ANG-453, anti-CTLA-4 Mab, AP-12009, aprepitant, aripiprazole, arsenic trioxide, astemizole, atlizumab, atomoxetine hydrochloride; Bevacizumab, BG-9928, BMS-188667, botulinum toxin type B, BufferGel; Caffeine, CDP-870, cetuximab, cilomilast, ciluprevir, clofarabine, continuous erythropoiesis receptor activator, CP-461; Darbepoetin alfa, deferasirox, desloratadine, desoxyepothilone B, diflomotecan, dolasetron, drotrecogin alfa (activated), duloxetine hydrochloride; ED-71, efalizumab, efaproxiral sodium, EKB-569, eletriptan, EMD-72000, enfuvirtide, erlotinib hydrochloride, escitalopram oxalate, etoricoxib; Fampridine, ferumoxytol, fondaparinux sodium; Gadofosveset sodium, gastrazole, gefitinib, gemtuzumab ozogamicin, gepirone hydrochloride glutamine; hLM609, HSPPC-96, human insulin; IDD-1, **imatinib mesylate**, indisulam, inhaled insulin, ixabepilone; Keratinocyte growth factor; Lapatinib, laquinimod, LDP-02, LE-SN38, levetiracetam, levosimendan, licofelone, liposomal doxorubicin, liposomal NDDP, lopinavir, lumiracoxib, LY-156735; Morphine hydrochloride, morphine-6-glucuronide, motexafin gadolinium, MS-27-275, MVA-5T4, MVA-Muc1-IL-2; Nemifitide ditriflutate, neridronic acid nitronaproxen, NSC-683864, NSC-703940, NVP-LAF-237; Oblimersen sodium, ocinaplon, oncomyc-NG, OPC-28326, ortataxel, ospemifene; Palonosetron hydrochloride, PEG-filgrastim peginterferon alfa-2(a), peginterferon alfa-2b, pegsunercept, pemetrexed disodium, pregabalin, prilocaine, pyridoxamine; RDP-58, recombinant glucagon-like peptide-1 (7-36) amide, recombinant human ApoA-I milano/phospholipid complex; SB-715992, soblidotin, sodium dichloroacetate, St. John's Wort extract; TAS-102, terfenadine, TG-1024, TG-5001, 4'-Thio-ara-C, tipranavir, topixantrone hydrochloride, trabectedin, transdermal selegiline, trimethoprim, **troxacitabine**, TT-232; Vatalanib succinate, vinflunine; Ximelagatran; Ziprasidone hydrochloride, Zoledronic acid monohydrate.

CT *Clinical Trials: SN, statistics & numerical data
*Databases, Factual: SN, statistics & numerical data
Humans
Statistics

L89 ANSWER 15 OF 54 MEDLINE on STN DUPLICATE 13

ACCESSION NUMBER:	2004035206 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 14735233
TITLE:	Gateways to clinical trials.
AUTHOR:	Bayes M; Rabasseda X; Prous J R
CORPORATE SOURCE:	Prous Science, Barcelona, Spain.. mbayes@prous.com
SOURCE:	Methods and findings in experimental and clinical pharmacology, (2003 Dec) 25 (10) 831-55. Journal code: 7909595. ISSN: 0379-0355.
PUB. COUNTRY:	Spain
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200404
ENTRY DATE:	Entered STN: 20040122 Last Updated on STN: 20040501 Entered Medline: 20040430

ED Entered STN: 20040122
Last Updated on STN: 20040501
Entered Medline: 20040430

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity, the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: Abetimus sodium, adalimumab, alefacept, alemtuzumab, almotriptan, AMGN-0007, anakinra, anti-CTLA-4 Mab, L-arginine hydrochloride, arzoxifene hydrochloride, astemizole, atazanavir sulfate, atlizumab; Belimumab, BG-9928, binodenoson, bosentan, botulinum toxin type B, bovine lactoferrin, BufferGel; Caspofungin acetate, ciclesonide,cilomilast, ciluprevir, clofarabine, CVT-3146; Darbepoetin alfa, desloratadine, diflomotecan, doripenem, dronedarone hydrochloride, drotrecogin alfa (activated), DT388-GM-CSF, duloxetine hydrochloride, E-5564, efalizumab, enfuvirtide, esomeprazole magnesium, estradiol acetate, ETC-642, exenatide, exisulind, ezetimib; Febuxostat; Gallium maltolate, ganirelix acetate, garenoxacin mesilate, gefitinib; H11, HuMax; IL-15, IDD-1, IGIV-C, **imatinib mesylate**, ISIS-14803, ITF-1697, ivabradine hydrochloride; KRN-5500; L-365260, levetiracetam, levosimendan, licofelone, linezolid, LJP-1082, lopinavir lumiracoxib; MCC-478, melatonin, morphine hydrochloride, morphine-6-glucuronide, moxidectin; N-Acetylcarnosine, natalizumab, NM-702, NNC-05-1869, NSC-703940; Ocinaplon OM-89, omalizumab, omeprazole/ sodium bicarbonate, OPC-28326, ospemifene; PEG-filgrastim peginterferon alfa-2a, pegsunercept, pirfenidone, pralmorelin, pregabalin; Recombinant glucagon-like peptide-1 (7-36) amide, repifermin, RSD-1235; S-8184, selodenoson, sodium dichloroacetate, suberanilohydroxamic acid; TAS-102, terfenadine, teriparatide, tipranavir **troxacitabine**; Ximelagatran; YM-337.

CT *Clinical Trials
*Drug Therapy
Humans

L89 ANSWER 16 OF 54 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2003053879 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12563614
TITLE: Advanced-phase chronic myeloid leukemia.
AUTHOR: Cortes Jorge; Kantarjian Hagop
CORPORATE SOURCE: Department of Leukemia, The University of Texas, M.D. Anderson Cancer Center, Houston, TX 77030, USA.
SOURCE: Seminars in hematology, (2003 Jan) 40 (1) 79-86. Ref: 70
Journal code: 0404514. ISSN: 0037-1963.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030204
Last Updated on STN: 20031009
Entered Medline: 20031008

ED Entered STN: 20030204
Last Updated on STN: 20031009
Entered Medline: 20031008

AB Chronic myeloid leukemia (CML) typically runs a biphasic or triphasic course, with diagnoses usually made in the chronic phase (CP). Without effective treatment, patients eventually progress to a blastic phase (BP),

frequently through an intermediate or accelerated phase (AP). Because the definition of AP varies among studies, comparisons of outcome and prognosis are difficult. The management of patients in these advanced phases of the disease has been much less satisfactory than that of patients in CP. Treatment with interferon-alfa (IFNalpha)-based therapy is ineffective for most patients in AP and for all of those in BP. **Imatinib mesylate** has demonstrated significant activity AP and BP disease, although the results are inferior compared to treatment in CP. In AP, 82% of patients achieve a hematologic response, with 24% achieving a major cytogenetic remission (MCR). Early MCR (within 3 months of diagnosis) provides a survival advantage over patients who do not achieve this response or achieve it later. In BP, 21% of previously treated patients and 36% of previously untreated patients have responded to imatinib, and up to 17% of patients may achieve a major cytogenetic response. However, responses are frequently short-lived. Several agents are being investigated for treatment of advanced-phase CML, including decitabine (DAC), homoharringtonine (HHT), **troxacitabine**, clofarabine, farnesyl transferase (FTase) inhibitors (FTI), and others. Many have also proven to be synergistic with imatinib in vitro and combination studies are ongoing. Continued investigation of these approaches is needed to improve the long-term prognosis of advanced-phase CML.

CT Antineoplastic Agents: TU, therapeutic use
Blast Crisis: PA, pathology
Humans
*Leukemia, Myeloid, Chronic: CL, classification
Leukemia, Myeloid, Chronic: PA, pathology
*Leukemia, Myeloid, Chronic: TH, therapy
Prognosis

CN 0 (Antineoplastic Agents)

L89 ANSWER 17 OF 54 MEDLINE on STN

ACCESSION NUMBER:	2002345081 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 12087878
TITLE:	Gateways to Clinical Trials.
AUTHOR:	Bayes M; Rabasseda X; Prous J R
SOURCE:	Methods and findings in experimental and clinical pharmacology, (2002 Apr) 24 (3) 159-84. Ref: 150 Journal code: 7909595. ISSN: 0379-0355.
PUB. COUNTRY:	Spain
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200301
ENTRY DATE:	Entered STN: 20020629 Last Updated on STN: 20030111 Entered Medline: 20030110

ED Entered STN: 20020629
Last Updated on STN: 20030111
Entered Medline: 20030110

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity, the world's first drug discovery and development portal, and provides information on study design, treatments, conclusions and references. This issue focuses on the following selection of drugs: Abiciximab, acetylcholine chloride, acetylcysteine, alefacept, alemtuzumab, alicaforsen, alteplase, aminopterin, amoxicillin sodium,

amphotericin B, anastrozole, argatroban monohydrate, arsenic trioxide, aspirin, atazanavir, atorvastatin, augmerosen, azathioprine; Benzylpenicillin, BMS-284756, botulinum toxin type A, botulinum toxin type B, BQ-123, budesonide, BXT-51072; Calcium folinate, carbamazepine, carboplatin, carmustine, ceftriaxone sodium, cefuroxime axetil, chorionic gonadotropin (human), cimetidine, ciprofloxacin hydrochloride, cisplatin, citalopram hydrobromide, cladribine, clarithromycin, clavulanic acid, clofarabine, clopidogrel hydrogensulfate, clotrimazole, CNI-1493, colesevelam hydrochloride, cyclophosphamide, cytarabine; Dalteparin sodium, daptomycin, darbepoetin alfa, debrisoquine sulfate, dexrazoxane, diaziquone, didanosine, docetaxel, donezepil, doxorubicin hydrochloride liposome injection, DX-9065a; Eberconazole, ecogramostim, eletriptan, enoxaparin sodium, epoetin, epoprostenol sodium, erlizumab, ertapenem sodium, ezetimibe; Fampridine, fenofibrate, filgrastim, fluconazole, fludarabine phosphate, fluorouracil, 5-fluorouracil/epinephrine, fondaparinux sodium, formoterol fumarate; Gabapentin, gemcitabine, gemfibrozil, glatiramer; Heparin sodium, homoharringtonine; Ibuprofen, iloprost, **imatinib mesilate**, imiquimod, interferon alpha-2b, interferon alpha-2c, interferon-beta; KW-6002; Lamotrigine, lanoteplase, metoprolol tartrate, mitoxantrone hydrochloride; Naproxen sodium, naratriptan, Natalizumab, nelfinavir mesilate, nevirapine, nifedipine, NSC-683864; Oral heparin; Paclitaxel, peginterferon alfa-2b, phenytoin, pimecrolimus, piperacillin, pleconaril, pramipexole hydrochloride, prednisone, pregabalin, progesterone; Rasburicase, ravuconazole, reteplase, ribavirin, rituximab, rizatriptan, rosiglitazone maleate, rotigotine; Semaxanib, sildenafil citrate, simvastatin, stavudine, sumatriptan; Tacrolimus, tamoxifen citrate, tanomastat, tazobactam, telithromycin, tenecteplase, tolafentrine, tolterodine tartrate, triamcinolone acetonide, trimetazidine, **troxacitabine**; Valproic acid, vancomycin hydrochloride, vincristine, voriconazole, Warfarin sodium; Ximelagatran, Zidovudine, zolmitriptan.

CT *Clinical Trials
*Drug Therapy
Humans

L89 ANSWER 18 OF 54 MEDLINE on STN
ACCESSION NUMBER: 2002687859 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12446421
TITLE: Chronic myelogenous leukemia.
AUTHOR: Druker Brian J; O'Brien Stephen G; Cortes Jorge; Radich Jerald
CORPORATE SOURCE: University of Newcastle, Royal Victoria Infirmary, Newcastle Upon Tyne, United Kingdom.
SOURCE: Hematology / the Education Program of the American Society of Hematology. American Society of Hematology. Education Program, (2002) 111-35. Ref: 173
Journal code: 100890099. ISSN: 1520-4391.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20021214
Last Updated on STN: 20030828
Entered Medline: 20030827

ED Entered STN: 20021214
Last Updated on STN: 20030828
Entered Medline: 20030827

AB The treatment options for chronic myelogenous leukemia (CML) continue to evolve rapidly. **Imatinib mesylate** (**Gleevec**, **Glivec**, formerly STI571) has continued to show remarkable clinical benefits and the updated results with this agent are reviewed. As relapses using single agent imatinib have occurred, particularly in advanced phase patients, the issue of whether combinations of other antileukemic agents with imatinib may yield improved results is addressed. In addition, data on new agents that have potential in the treatment of CML are reviewed. These agents are presented in the context of their molecular mechanism of action. The most recent data for stem cell transplantation, along with advances in nonmyeloablative transplants, are also reviewed. In Section I, Drs. Stephen O'Brien and Brian Druker update the current status of clinical trials with imatinib and review ongoing investigations into mechanisms of resistance and combinations of imatinib with other agents. They also present their views on integration of imatinib with other therapies. In Section II, Dr. Jorge Cortes describes the most recent data on novel therapies for CML, including farnesyl transferase inhibitors, arsenic trioxide, decitabine, and **troxatyl**, among others. These agents are discussed in the context of their molecular mechanism of action and rationale for use. In Section III, Dr. Jerald Radich updates the results of stem cell transplants for CML, including emerging data on nonmyeloablative transplants. He also presents data on using microarrays to stratify patients into molecularly defined risk groups.

CT *Antineoplastic Agents: TU, therapeutic use
Clinical Trials
*Hematopoietic Stem Cell Transplantation: MT, methods
Hematopoietic Stem Cell Transplantation: MO, mortality
Humans
Leukemia, Myeloid, Chronic: MO, mortality
*Leukemia, Myeloid, Chronic: TH, therapy
Piperazines: AD, administration & dosage
Piperazines: TU, therapeutic use
Pyrimidines: AD, administration & dosage
Pyrimidines: TU, therapeutic use
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Survival Analysis

RN 152459-95-5 (imatinib)

CN 0 (Antineoplastic Agents); 0 (Piperazines); 0 (Pyrimidines)

L89 ANSWER 19 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 15

ACCESSION NUMBER: 2001380875 EMBASE
TITLE: Chronic myelogenous leukemia.
AUTHOR: Kalidas M.; Kantarjian H.; Talpaz M.
CORPORATE SOURCE: Dr. M. Talpaz, Department of Bioimmunotherapy, M.D. Anderson Cancer Center, Box 422, 1515 Holcombe Blvd, Houston, TX 77030, United States. mtalpaz@mail.mdanderson.org
SOURCE: Journal of the American Medical Association, (22 Aug 2001) 286/8 (895-898).
Refs: 48
ISSN: 0098-7484 CODEN: JAMAAP
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
025 Hematology
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English
CT Medical Descriptors:
*chronic myeloid leukemia: DT, drug therapy
*chronic myeloid leukemia: ET, etiology
*chronic myeloid leukemia: TH, therapy
pathophysiology
Philadelphia 1 chromosome
karyotype
fluorescence in situ hybridization
reverse transcription polymerase chain reaction
malignant transformation
stem cell transplantation
fever: SI, side effect
chill: SI, side effect
fatigue: SI, side effect
arthralgia: SI, side effect
anorexia: SI, side effect
weight reduction
nausea: SI, side effect
vomiting: SI, side effect
fluid retention
human
review
priority journal
Drug Descriptors:
*BCR ABL protein: EC, endogenous compound
*busulfan: AE, adverse drug reaction
*busulfan: DT, drug therapy
*hydroxyurea: AE, adverse drug reaction
*hydroxyurea: CB, drug combination
*hydroxyurea: DT, drug therapy
*alpha interferon: AE, adverse drug reaction
*alpha interferon: CB, drug combination
*alpha interferon: DT, drug therapy
*2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: AE, adverse drug reaction
*2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: DT, drug therapy
protein tyrosine kinase: EC, endogenous compound
messenger RNA: EC, endogenous compound
homoharringtonine: DT, drug therapy
5 aza 2' deoxycytidine: DT, drug therapy
troxacitabine: DT, drug therapy
cytosine derivative: DT, drug therapy
vaccine: DT, drug therapy
cytarabine: AE, adverse drug reaction
cytarabine: CB, drug combination
cytarabine: DT, drug therapy
protein tyrosine kinase inhibitor: AE, adverse drug reaction
protein tyrosine kinase inhibitor: DT, drug therapy
unclassified drug
gleevec
RN (busulfan) 55-98-1; (hydroxyurea) 127-07-1; (2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine) 152459-95-5; (protein **tyrosine kinase**) 80449-02-1; (homoharringtonine) 26833-87-4; (5 aza 2' deoxycytidine) 2353-33-5; (cytarabine) 147-94-4, 69-74-9
CN **(1) Sti 571**; **(2) Gleevec**; (3) Cgp 57148
CO (2) Novartis (United States); (3) Novartis (Switzerland)

L89 ANSWER 20 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2004366355 EMBASE
TITLE: Imatinib therapy in chronic myelogenous leukemia: Strategies to avoid and overcome resistance.
AUTHOR: Hochhaus A.; La Rosee P.
CORPORATE SOURCE: Prof. A. Hochhaus, III Medizinische Klinik, Fakultat Klinische Medizin Mannheim, Universitat Heidelberg, Wiesbadener Strasse 7-11, Mannheim 68305, Germany. hochhaus@uni-hd.de
SOURCE: Leukemia, (2004) 18/8 (1321-1331).
Refs: 109
ISSN: 0887-6924 CODEN: LEUKED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Imatinib is a molecularly targeted therapy that inhibits the oncogenic fusion protein BCR-ABL, the **tyrosine kinase** involved in the pathogenesis of chronic myelogenous leukemia (CML). Selective inhibition of BCR-ABL activity by imatinib has demonstrated efficacy in the treatment of CML, particularly in chronic phase. Some patients, however, primarily those with advanced disease, are either refractory to imatinib or eventually relapse. Relapse with imatinib frequently depends not only on re-emergence of BCR-ABL kinase activity but may also indicate BCR-ABL-independent disease progression not amenable to imatinib inhibition. Results from phase 2/3 trials suggest that rates of resistance and relapse correlate with the stage of disease and with the monitoring parameters - hematologic, cytogenetic and molecular response. These observations and more recent trials with imatinib, combined with insights provided by an increased understanding of the molecular mechanisms of resistance, have established the rationale for strategies to avoid and overcome imatinib resistance in the management of CML patients. To prevent resistance, early diagnosis and prompt treatment with appropriate initial dosing is essential. Management of resistance may include therapeutic strategies such as dose escalation to achieve individual optimal levels, combination therapy, as well as treatment interruption. .COPYRGT. 2004 Nature Publishing Group All rights reserved.

CT Medical Descriptors:
*chronic myeloid leukemia: DI, diagnosis
*chronic myeloid leukemia: DR, drug resistance
*chronic myeloid leukemia: DT, drug therapy
*chronic myeloid leukemia: ET, etiology
*chronic myeloid leukemia: TH, therapy
drug targeting
protein targeting
drug efficacy
enzyme activity
cancer recurrence
cancer staging
drug response
chromosome analysis
monotherapy
advanced cancer: DI, diagnosis
advanced cancer: DR, drug resistance

advanced cancer: DT, drug therapy
advanced cancer: ET, etiology
minimal residual disease: CO, complication
polymerase chain reaction
gene amplification
gene mutation
cancer survival
amino acid substitution
drug dose regimen
maximum tolerated dose
drug blood level
drug mechanism
low drug dose
allogeneic hematopoietic stem cell transplantation
human
clinical trial
review
nucleotide sequence
priority journal
Drug Descriptors:
*imatinib: CT, clinical trial
*imatinib: CB, drug combination
*imatinib: CR, drug concentration
*imatinib: DO, drug dose
*imatinib: DT, drug therapy
*imatinib: PD, pharmacology
BCR ABL protein: EC, endogenous compound
orosomucoid: EC, endogenous compound
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
peginterferon: CT, clinical trial
peginterferon: CB, drug combination
peginterferon: DT, drug therapy
alpha2a interferon: CT, clinical trial
alpha2a interferon: CB, drug combination
alpha2a interferon: DT, drug therapy
alpha2b interferon: CT, clinical trial
alpha2b interferon: CB, drug combination
alpha2b interferon: DT, drug therapy
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: CM, drug comparison
etoposide: DT, drug therapy
arsenic trioxide: CT, clinical trial
arsenic trioxide: CB, drug combination
arsenic trioxide: DT, drug therapy
gemtuzumab ozogamicin: CT, clinical trial
gemtuzumab ozogamicin: CB, drug combination
gemtuzumab ozogamicin: DT, drug therapy
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
idarubicin: CT, clinical trial
idarubicin: CB, drug combination
idarubicin: DT, drug therapy
cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination

cyclophosphamide: DT, drug therapy
vincristine: CT, clinical trial
vincristine: CM, drug comparison
vincristine: DT, drug therapy
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
dexamethasone: CT, clinical trial
dexamethasone: CB, drug combination
dexamethasone: DT, drug therapy
homoharringtonine: CT, clinical trial
homoharringtonine: CB, drug combination
homoharringtonine: DT, drug therapy
tipifarnib: CT, clinical trial
tipifarnib: CB, drug combination
tipifarnib: DT, drug therapy
bortezomib: CT, clinical trial
bortezomib: CB, drug combination
bortezomib: DT, drug therapy
hydroxyurea: CT, clinical trial
hydroxyurea: CB, drug combination
hydroxyurea: DT, drug therapy
troxacitabine: CT, clinical trial
troxacitabine: CB, drug combination
troxacitabine: DT, drug therapy
lonafarnib: CT, clinical trial
lonafarnib: CB, drug combination
lonafarnib: DT, drug therapy
5 aza 2' deoxycytidine: CT, clinical trial
5 aza 2' deoxycytidine: CB, drug combination
5 aza 2' deoxycytidine: DT, drug therapy

RN (imatinib) 152459-95-5, **220127-57-1**; (orosomucoid) 79921-18-9; (cytarabine) 147-94-4, 69-74-9; (alpha2a interferon) 76543-88-9; (alpha2b interferon) 99210-65-8; (etoposide) 33419-42-0; (arsenic trioxide) 1303-24-8, 1327-53-3, 13464-58-9, 15502-74-6; (mitoxantrone) 65271-80-9, 70476-82-3; (idarubicin) 57852-57-0, 58957-92-9; (cyclophosphamide) 50-18-0; (vincristine) 57-22-7; (doxorubicin) 23214-92-8, 25316-40-9; (dexamethasone) 50-02-2; (homoharringtonine) 26833-87-4; (tipifarnib) 192185-72-1; (bortezomib) 179324-69-7, 197730-97-5; (hydroxyurea) 127-07-1; (**troxacitabine**) **145918-75-8**; (lonafarnib) 193275-84-2; (5 aza 2' deoxycytidine) 2353-33-5

CN **(1) Glivec; (2) Gleevec; (3) Sti 571**

CO (3) Novartis (Switzerland)

GEN GENBANK AAB60394 referred number; GENBANK M14752 referred number

L89 ANSWER 21 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004228259 EMBASE

TITLE: t(8;21)(q22;q22) in blast phase of chronic myelogenous leukemia.

AUTHOR: Yin C.C.; Medeiros L.J.; Glassman A.B.; Lin P.

CORPORATE SOURCE: Dr. P. Lin, Dept. of Hematopathology, Box 72, UT M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, United States

SOURCE: American Journal of Clinical Pathology, (2004) 121/6 (836-842).
Refs: 28
ISSN: 0002-9173 CODEN: AJCPAI

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The blast phase of chronic myelogenous leukemia (CML) frequently is associated with cytogenetic evidence of clonal evolution, defined as chromosomal aberrations in addition to the t(9;22)(q34;q11.2). We identified the t(8;21)(q22;q22) and other cytogenetic abnormalities by conventional cytogenetics and fluorescence in situ hybridization in 2 patients with t(9;22)-positive CML at the time of blast phase. The t(8;21), which typically is associated with a distinct subtype of de novo acute myeloid leukemia (AML) carrying the am11/eto fusion gene, was accompanied by increased bone marrow myeloblasts (33%) in case 1 and extramedullary myeloid sarcoma in case 2, suggesting its possible role in disease progression. In case 1, the leukemic cells in aspirate smears had salmon-colored cytoplasmic granules, and immunophenotypic studies showed that the blasts expressed CD19. These findings suggest that the pathologic features of blast phase CML with the t(8;21) resemble those of de novo AML with the t(8;21).

CT Medical Descriptors:
*chronic myeloid leukemia: DI, diagnosis
*chronic myeloid leukemia: DT, drug therapy
*chronic myeloid leukemia: SU, surgery
*chromosome 22q
*myeloblast
disease association
cytogenetics
cell clone
chromosome aberration
fluorescence in situ hybridization
bone marrow
sarcoma
cancer growth
color
cytoplasm
chromosome 8
chromosome 21
clinical feature
cancer combination chemotherapy
cancer surgery
stem cell transplantation
treatment outcome
human
male
female
case report
human tissue
adult
article
priority journal
Drug Descriptors:
troxacitabine: DT, drug therapy
imatinib: CB, drug combination
imatinib: DT, drug therapy
alpha interferon: CB, drug combination
alpha interferon: DT, drug therapy
cytarabine: CM, drug comparison

cytarabine: DT, drug therapy
RN (**troxacitabine**) **145918-75-8**; (imatinib) 152459-95-5, **220127-57-1**; (cytarabine) 147-94-4, 69-74-9

L89 ANSWER 22 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004318012 EMBASE
TITLE: Accelerated and blastic phases of chronic myelogenous leukemia.
AUTHOR: Giles F.J.; Cortes J.E.; Kantarjian H.M.; O'Brien S.M.
CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, The University of Texas, M.D. Anderson Cancer Ctr., 1515 H., Houston, TX, United States. fgiles@mdanderson.org
SOURCE: Hematology/Oncology Clinics of North America, (2004) 18/3 (753-774).
Refs: 177
ISSN: 0889-8588 CODEN: HCNAEQ
PUBLISHER IDENT.: S 0889-8588(04)00010-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although the mechanisms of CML transformation remain poorly understood, recent therapeutic advances moderately have improved the prognosis of patients in AP and BP. Treatment with IFN-αbased regimens are minimally effective for patients in AP and ineffective for those in BP. **Imatinib mesylate** has a significant but generally transient response rate in patients in AP and BP. Hope for progress in this area lies mainly in the development of novel targeted therapies. The more promising agents that are being investigated include decitabine, HHT, **troxacitabine**, clofarabine, farnesyl transferase inhibitors, histone deacetylase inhibitors, and the VEGF and mTOR inhibitors. Many of these approaches may be synergistic with imatinib or the more powerful abl or Src inhibitors that are in development.
CT Medical Descriptors:
*blast cell crisis
*chronic myeloid leukemia: DT, drug therapy
cell cycle
prognosis
cancer survival
drug efficacy
treatment failure
diagnostic procedure
treatment outcome
basophil
thrombocyte count
cytogenetics
laboratory test
drug dose regimen
high risk population
cancer risk
risk assessment
DNA methylation
Southern blotting
bone marrow suppression: SI, side effect
side effect: SI, side effect

mortality
drug cytotoxicity: SI, side effect
stomatitis: SI, side effect
hand foot syndrome: SI, side effect
drug eruption: SI, side effect
human
clinical trial
review
priority journal
Drug Descriptors:
5 aza 2' deoxycytidine: AE, adverse drug reaction
5 aza 2' deoxycytidine: CT, clinical trial
5 aza 2' deoxycytidine: CB, drug combination
5 aza 2' deoxycytidine: DT, drug therapy
troxacitabine: AE, adverse drug reaction
troxacitabine: CT, clinical trial
troxacitabine: CB, drug combination
troxacitabine: DT, drug therapy
protein farnesyltransferase inhibitor: AE, adverse drug reaction
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: CB, drug combination
protein farnesyltransferase inhibitor: DT, drug therapy
histone deacetylase inhibitor: AE, adverse drug reaction
histone deacetylase inhibitor: CT, clinical trial
histone deacetylase inhibitor: CB, drug combination
histone deacetylase inhibitor: DT, drug therapy
vasculotropin inhibitor: AE, adverse drug reaction
vasculotropin inhibitor: CT, clinical trial
vasculotropin inhibitor: CB, drug combination
vasculotropin inhibitor: DT, drug therapy
hydroxyurea: AE, adverse drug reaction
hydroxyurea: CT, clinical trial
hydroxyurea: CB, drug combination
hydroxyurea: DT, drug therapy
daunorubicin: AE, adverse drug reaction
daunorubicin: CT, clinical trial
daunorubicin: CB, drug combination
daunorubicin: DT, drug therapy
cytarabine: AE, adverse drug reaction
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: DT, drug therapy
recombinant alpha interferon: AE, adverse drug reaction
recombinant alpha interferon: CT, clinical trial
recombinant alpha interferon: CB, drug combination
recombinant alpha interferon: DT, drug therapy
peginterferon: AE, adverse drug reaction
peginterferon: CT, clinical trial
peginterferon: CB, drug combination
peginterferon: DT, drug therapy
idarubicin: AE, adverse drug reaction
idarubicin: CT, clinical trial
idarubicin: CB, drug combination
idarubicin: DT, drug therapy
arsenic trioxide: AE, adverse drug reaction
arsenic trioxide: CT, clinical trial
arsenic trioxide: CB, drug combination
arsenic trioxide: DT, drug therapy
lonafarnib: AE, adverse drug reaction
lonafarnib: CT, clinical trial

lonafarnib: CB, drug combination
lonafarnib: DT, drug therapy
tipifarnib: AE, adverse drug reaction
tipifarnib: CT, clinical trial
tipifarnib: CB, drug combination
tipifarnib: DT, drug therapy
retinoid derivative: AE, adverse drug reaction
retinoid derivative: CT, clinical trial
retinoid derivative: CB, drug combination
retinoid derivative: DT, drug therapy
nucleoside analog: AE, adverse drug reaction
nucleoside analog: CT, clinical trial
nucleoside analog: CB, drug combination
nucleoside analog: DT, drug therapy
doxorubicin: AE, adverse drug reaction
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
vincristine: AE, adverse drug reaction
vincristine: CT, clinical trial
vincristine: CB, drug combination
vincristine: DT, drug therapy
etoposide: AE, adverse drug reaction
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: DT, drug therapy
bevacizumab: AE, adverse drug reaction
bevacizumab: CT, clinical trial
bevacizumab: CB, drug combination
bevacizumab: DT, drug therapy
mitoxantrone: AE, adverse drug reaction
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
semaxanib: AE, adverse drug reaction
semaxanib: CT, clinical trial
semaxanib: CB, drug combination
semaxanib: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CB, drug combination
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
vatalanib: AE, adverse drug reaction
vatalanib: CT, clinical trial
vatalanib: CB, drug combination
vatalanib: DT, drug therapy
rapamycin 2,2 bis(hydroxymethyl)propionate: AE, adverse drug reaction
rapamycin 2,2 bis(hydroxymethyl)propionate: CT, clinical trial
rapamycin 2,2 bis(hydroxymethyl)propionate: CB, drug combination
rapamycin 2,2 bis(hydroxymethyl)propionate: DT, drug therapy
everolimus: AE, adverse drug reaction
everolimus: CT, clinical trial
everolimus: CB, drug combination
everolimus: DT, drug therapy
rapamycin derivative: AE, adverse drug reaction
rapamycin derivative: CT, clinical trial

rapamycin derivative: CB, drug combination
rapamycin derivative: DT, drug therapy
ap 23573: AE, adverse drug reaction
ap 23573: CT, clinical trial
ap 23573: CB, drug combination
ap 23573: DT, drug therapy
arylbutyric acid derivative: AE, adverse drug reaction
arylbutyric acid derivative: CT, clinical trial
arylbutyric acid derivative: CB, drug combination
arylbutyric acid derivative: DT, drug therapy
unindexed drug
unclassified drug
imatinib
lbh 589

RN (5 aza 2' deoxycytidine) 2353-33-5; (**troxacitabine**) **145918-75-8**; (hydroxyurea) 127-07-1; (daunorubicin) 12707-28-7, 20830-81-3, 23541-50-6; (cytarabine) 147-94-4, 69-74-9; (idarubicin) 57852-57-0, 58957-92-9; (arsenic trioxide) 1303-24-8, 1327-53-3, 13464-58-9, 15502-74-6; (lonafarnib) 193275-84-2; (tipifarnib) 192185-72-1; (doxorubicin) 23214-92-8, 25316-40-9; (vincristine) 57-22-7; (etoposide) 33419-42-0; (bevacizumab) 216974-75-3; (mitoxantrone) 65271-80-9, 70476-82-3; (semaxanib) 186610-95-7; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (vatalanib) 212141-54-3, 212142-18-2; (rapamycin 2,2 bis(hydroxymethyl)propionate) 162635-04-3, 343261-52-9; (everolimus) 159351-69-6; (imatinib) 152459-95-5, **220127-57-1**

CN **Sti 571**; Sch 66336; R 115777; Su 5416; Su 6668; Ptk 787; Cci 779; Rad 001; Ap 23573; Lbh 589

L89 ANSWER 23 OF 54 EMBASE
on STN

ACCESSION NUMBER: 2004268142 EMBASE
TITLE: **Imatinib mesylate** in the treatment of chronic myelogenous leukemia.
AUTHOR: Borthakur G.; Cortes J.E.
CORPORATE SOURCE: Dr. J.E. Cortes, Department of Leukemia, Univ. TX M. D. Anderson Cancer Ctr., Box 0428, 1515 Holcombe Blvd, Houston, TX 77030, United States. jcortes@mdanderson.org
SOURCE: International Journal of Hematology, (2004) 79/5 (411-419). Refs: 69
ISSN: 0925-5710 CODEN: IJHEEY
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Imatinib mesylate** binds to the inactive conformation of BCR-ABL **tyrosine kinase**, suppressing the Philadelphia chromosome-positive clone in chronic myelogenous leukemia (CML). Clinical studies of imatinib have yielded impressive results in the treatment of all phases of CML. With the higher rates of complete cytogenetic response with imatinib, molecular monitoring of disease has become mandatory in assessing response and determining prognosis. The practical aspects of the treatment of CML with imatinib are discussed. The emergence of imatinib resistance, albeit in a small percentage of patients, has prompted an evaluation of innovative treatment strategies. .COPYRGT. 2004 The Japanese Society of Hematology.

CT Medical Descriptors:
*chronic myeloid leukemia: DR, drug resistance
*chronic myeloid leukemia: DT, drug therapy
drug binding
enzyme conformation
Philadelphia 1 chromosome
cytogenetics
drug response
drug monitoring
bone marrow suppression: SI, side effect
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
anemia: SI, side effect
cardiotoxicity: SI, side effect
fatigue: SI, side effect
bone pain: DT, drug therapy
bone pain: SI, side effect
liver toxicity: SI, side effect
rash: SI, side effect
nausea: DT, drug therapy
nausea: SI, side effect
vomiting: DT, drug therapy
vomiting: SI, side effect
edema: DT, drug therapy
edema: SI, side effect
muscle cramp: SI, side effect
arthralgia: SI, side effect
diarrhea: DT, drug therapy
diarrhea: SI, side effect
lung edema: DT, drug therapy
lung edema: SI, side effect
drug mechanism
human
clinical trial
review
Drug Descriptors:
*imatinib: AE, adverse drug reaction
*imatinib: CT, clinical trial
*imatinib: CB, drug combination
*imatinib: CM, drug comparison
*imatinib: DT, drug therapy
*imatinib: PD, pharmacology
BCR ABL protein
protein tyrosine kinase inhibitor
interferon: CT, clinical trial
interferon: CB, drug combination
interferon: CM, drug comparison
interferon: DT, drug therapy
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
vincristine: CB, drug combination
vincristine: DT, drug therapy
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
dexamethasone: CB, drug combination

dexamethasone: DT, drug therapy
prochlorperazine: DT, drug therapy
omeprazole: DT, drug therapy
ondansetron: DT, drug therapy
loperamide: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
diuretic agent: DT, drug therapy
tyrphostin: PD, pharmacology
adaphostin: PD, pharmacology
protein farnesyltransferase inhibitor: PD, pharmacology
tipifarnib: PD, pharmacology
lonafarnib: PD, pharmacology
5 aza 2' deoxycytidine: DT, drug therapy
5 aza 2' deoxycytidine: PD, pharmacology
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
homoharringtonine: CB, drug combination
homoharringtonine: DV, drug development
troxacitabine: DV, drug development
proteasome inhibitor: DV, drug development
geldanamycin: PD, pharmacology
alpha2a interferon: CB, drug combination
alpha2a interferon: DT, drug therapy
alpha2b interferon: CB, drug combination
alpha2b interferon: DT, drug therapy
arsenic trioxide: CB, drug combination
unclassified drug
peginterferon alpha2a

RN (imatinib) 152459-95-5, **220127-57-1**; (cytarabine) 147-94-4, 69-74-9; (cyclophosphamide) 50-18-0; (vincristine) 57-22-7; (doxorubicin) 23214-92-8, 25316-40-9; (dexamethasone) 50-02-2; (prochlorperazine) 58-38-8; (omeprazole) 73590-58-6, 95510-70-6; (ondansetron) 103639-04-9, 116002-70-1, 99614-01-4; (loperamide) 34552-83-5, 53179-11-6; (tipifarnib) 192185-72-1; (lonafarnib) 193275-84-2; (5 aza 2' deoxycytidine) 2353-33-5; (homoharringtonine) 26833-87-4; (**troxacitabine**) **145918-75-8**; (geldanamycin) 30562-34-6; (alpha2a interferon) 76543-88-9; (alpha2b interferon) 99210-65-8; (arsenic trioxide) 1303-24-8, 1327-53-3, 13464-58-9, 15502-74-6; (peginterferon alpha2a) 198153-51-4
CN (1) Pegasys; R115777; Sch66336
CO (1) Hoffmann La Roche (United States)

L89 ANSWER 24 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004424349 EMBASE
TITLE: [News from the ASCO 2004 by localizations - Studies in phase I].
ACTUALITE DE L'ASCO 2004 PAR LOCALISATIONS - ETUDES DE PHASE I.
AUTHOR: Zanetta S.
CORPORATE SOURCE: S. Zanetta, Centre Georges-Francois-Leclerc, 1, rue du Pr Marion, F-21000 Dijon, France
SOURCE: Oncologie, (2004) 6/5 (365-368).
ISSN: 1292-3818 CODEN: OOLOFG
COUNTRY: France
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
CT Medical Descriptors:

*cancer chemotherapy
bone marrow suppression: SI, side effect
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
infection: SI, side effect
fatigue: SI, side effect
neurotoxicity: SI, side effect
malaise: SI, side effect
febrile neutropenia: SI, side effect
diarrhea: SI, side effect
chemotherapy induced emesis: SI, side effect
sepsis: SI, side effect
abdominal pain: SI, side effect
constipation: SI, side effect
anemia: SI, side effect
drug hypersensitivity: SI, side effect
liver dysfunction: SI, side effect
hyperglycemia: SI, side effect
dehydration: SI, side effect
hyponatremia: SI, side effect
rash: SI, side effect
skin toxicity: SI, side effect
mucosa inflammation: SI, side effect
peripheral neuropathy: SI, side effect
stomatitis: SI, side effect
hypertension: SI, side effect
thrombosis: SI, side effect
insomnia: SI, side effect
hypokalemia: SI, side effect
kidney failure: SI, side effect
respiration depression: SI, side effect
blood toxicity: SI, side effect
side effect: SI, side effect
urticaria: SI, side effect
hypovolemia: SI, side effect
hypotension: SI, side effect
edema: SI, side effect
human
conference paper
Drug Descriptors:
lapatinib: AE, adverse drug reaction
histone deacetylase inhibitor: AE, adverse drug reaction
indisulam: AE, adverse drug reaction
indisulam: IV, intravenous drug administration
troxacitabine: AE, adverse drug reaction
troxacitabine: IV, intravenous drug administration
nucleoside analog: AE, adverse drug reaction
nucleoside analog: IV, intravenous drug administration
exatecan: AE, adverse drug reaction
exatecan: IV, intravenous drug administration
paclitaxel: AE, adverse drug reaction
paclitaxel: IV, intravenous drug administration
ixabepilone: AE, adverse drug reaction
ixabepilone: IV, intravenous drug administration
imatinib: AE, adverse drug reaction
imatinib: CB, drug combination
gefitinib: AE, adverse drug reaction
gefitinib: CB, drug combination
erlotinib: AE, adverse drug reaction
erlotinib: CB, drug combination

n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6
quinazolinyl]acrylamide: AE, adverse drug reaction
n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6
quinazolinyl]acrylamide: CB, drug combination
3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
isothiazolecarboxamide: AE, adverse drug reaction
3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
isothiazolecarboxamide: CB, drug combination
vatalanib: AE, adverse drug reaction
vatalanib: CB, drug combination
7 hydroxystaurosporine: AE, adverse drug reaction
7 hydroxystaurosporine: CB, drug combination
gene expression modulator 231: AE, adverse drug reaction
gene expression modulator 231: CB, drug combination
bortezomib: AE, adverse drug reaction
bortezomib: CB, drug combination
lonafarnib: AE, adverse drug reaction
lonafarnib: CB, drug combination
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
thienylsulfonyl) 1h 1,4 benzodiazepine: AE, adverse drug reaction
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
thienylsulfonyl) 1h 1,4 benzodiazepine: CB, drug combination
everolimus: AE, adverse drug reaction
tariquidar: AE, adverse drug reaction
tariquidar: CB, drug combination
elacridar: AE, adverse drug reaction
elacridar: CB, drug combination
retinoid: AE, adverse drug reaction
epothilone B: AE, adverse drug reaction
epothilone B: IV, intravenous drug administration
discodermolide: AE, adverse drug reaction
discodermolide: PO, oral drug administration
taxane derivative: AE, adverse drug reaction
taxane derivative: PO, oral drug administration
alkylating agent: AE, adverse drug reaction
alkylating agent: IV, intravenous drug administration
DNA topoisomerase inhibitor: AE, adverse drug reaction
DNA topoisomerase inhibitor: IV, intravenous drug administration
docetaxel: CB, drug combination
unindexed drug
cp 4055
vnp 40101m
XK 469
mac 321
ai 850
bms 275183
dj 927
kos 906
t 138067
abt 751
xaa 296a
sb 715992
emd 72000
ag 2037
mbt 0206
bay 439006
abt 510

RN (lapatinib) 388082-78-8, 437755-78-7; (indisulam) 165668-41-7; (**troxacitabine**) **145918-75-8**; (exatecan) 197720-53-9; (paclitaxel) 33069-62-4; (ixabepilone) 219989-84-1; (imatinib)

152459-95-5, **220127-57-1**; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (erlotinib) 183319-69-9, 183321-74-6; (n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6 quinazolinyl]acrylamide) 267243-28-7, 338796-35-3; (3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide) 252003-65-9; (vatalanib) 212141-54-3, 212142-18-2; (7 hydroxystaurosporine) 112953-11-4; (bortezomib) 179324-69-7, 197730-97-5; (lonafarnib) 193275-84-2; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (everolimus) 159351-69-6; (tariquidar) 206873-63-4; (elacridar) 143664-11-3; (epothilone B) 152044-54-7; (discodermolide) 127943-53-7, 154335-30-5, 194232-29-6; (docetaxel) 114977-28-5

CN Gw 572016; Cp 4055; Dx 8951f; E 7070; Bms 247550; Abi 007; **Gleevec** ; Zd 1839; Osi 774; Ci 1033; Cp 547632; Ptk 787; Zk 222584; Ucn 01; GEM 231; Sch 66336; Bms 214662; Rad 001; Vnp 40101m; XK 469; Mac 321; Ai 850; Bms 275183; Dj 927; Epo 906; Kos 906; T 138067; Abt 751; Xaa 296a; Sb 715992; Emd 72000; Ag 2037; Mbt 0206; Bay 439006; Abt 510

L89 ANSWER 25 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004165534 EMBASE
TITLE: Novel therapies for patients with chronic myeloid leukemia.
AUTHOR: Giles F.J.; Kantarjian H.; Cortes J.
CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, University of Texas, MD Anderson Cancer Center, 1400 Holcombe Boulevard, Houston, TX 77030, United States. frankgiles@aol.com
SOURCE: Expert Review of Anticancer Therapy, (2004) 4/2 (271-282). Refs: 177
ISSN: 1473-7140 CODEN: ERATBJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The most immediate issues that will have a major impact on the long-term survival of patients with chronic myeloid leukemia is the optimal use of **imatinib mesylate** (**Gleevec.**RTM., Novartis) and the development of effective therapies for those patients who are intolerant of, or become resistant to, optimal doses of this agent. Of the multiple new agents that are currently being developed for patients with chronic myeloid leukemia, most are being investigated in patients who have developed resistance to imatinib, which is a confounding factor in itself. The mechanisms of action of novel agents are diverse and they may have a variably synergistic therapeutic relationship with imatinib. The complete blockade of the intracellular pathways that are triggered by Bcr-Abl, combined with successful reversal of apoptotic and/or angiogenic abnormalities in chronic myeloid leukemia, may well lead to a cure for the majority of patients. .COPYRGT. Future Drugs Ltd. All rights reserved.

CT Medical Descriptors:
*chronic myeloid leukemia: DR, drug resistance
*chronic myeloid leukemia: DT, drug therapy
survival time
drug use
drug research
drug efficacy
drug hypersensitivity: SI, side effect

cancer resistance
optimal drug dose
drug mechanism
drug potentiation
apoptosis
angiogenesis
cancer patient
dose response
DNA methylation
bone marrow suppression: SI, side effect
fever: SI, side effect
drug metabolism
human
nonhuman
clinical trial
review
Drug Descriptors:
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DV, drug development
*antineoplastic agent: DO, drug dose
*antineoplastic agent: IT, drug interaction
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PK, pharmacokinetics
*antineoplastic agent: PD, pharmacology
*antineoplastic agent: IV, intravenous drug administration
*antineoplastic agent: PO, oral drug administration
imatinib: AE, adverse drug reaction
imatinib: CT, clinical trial
imatinib: CB, drug combination
imatinib: CM, drug comparison
imatinib: DO, drug dose
imatinib: IT, drug interaction
imatinib: DT, drug therapy
imatinib: PD, pharmacology
BCR ABL protein: EC, endogenous compound
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: CM, drug comparison
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
cytarabine: PK, pharmacokinetics
cytarabine: PD, pharmacology
azacitidine: CB, drug combination
azacitidine: DT, drug therapy
azacitidine: PD, pharmacology
5 aza 2' deoxycytidine: AE, adverse drug reaction
5 aza 2' deoxycytidine: CB, drug combination
5 aza 2' deoxycytidine: DO, drug dose
5 aza 2' deoxycytidine: IT, drug interaction
5 aza 2' deoxycytidine: DT, drug therapy
5 aza 2' deoxycytidine: PD, pharmacology
etoposide: CB, drug combination
etoposide: DT, drug therapy

etoposide: PD, pharmacology
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
mitoxantrone: PD, pharmacology
histone deacetylase inhibitor: CB, drug combination
histone deacetylase inhibitor: IT, drug interaction
histone deacetylase inhibitor: DT, drug therapy
histone deacetylase inhibitor: PD, pharmacology
suberoylanilide hydroxamic acid: CB, drug combination
suberoylanilide hydroxamic acid: IT, drug interaction
suberoylanilide hydroxamic acid: DT, drug therapy
suberoylanilide hydroxamic acid: PD, pharmacology
depsipeptide: PD, pharmacology
hydroxamic acid derivative: PD, pharmacology
4 [n (2 hydroxyethyl) n [2 (3 indolyl)ethyl]aminomethyl]cinnamohydroxamic acid: PD, pharmacology
protein p21: EC, endogenous compound
protein p27: EC, endogenous compound
vasculotropin: EC, endogenous compound
bevacizumab: CB, drug combination
bevacizumab: DT, drug therapy
bevacizumab: PD, pharmacology
vasculotropin antibody: CB, drug combination
vasculotropin antibody: DT, drug therapy
vasculotropin antibody: PD, pharmacology
monoclonal antibody: CB, drug combination
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: CB, drug combination
protein tyrosine kinase inhibitor: DO, drug dose
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PD, pharmacology
protein tyrosine kinase inhibitor: IV, intravenous drug administration
protein tyrosine kinase inhibitor: PO, oral drug administration
ag 013736: CT, clinical trial
ag 013736: DT, drug therapy
ag 013736: PD, pharmacology
vatalanib: CT, clinical trial
vatalanib: CB, drug combination
vatalanib: DT, drug therapy
vatalanib: PD, pharmacology
vatalanib: PO, oral drug administration
n benzoylstaurosporine: DT, drug therapy
n benzoylstaurosporine: PD, pharmacology
semaxanib: DO, drug dose
semaxanib: DT, drug therapy
semaxanib: PD, pharmacology
semaxanib: IV, intravenous drug administration
phthalazine derivative: CT, clinical trial
phthalazine derivative: CB, drug combination
phthalazine derivative: DT, drug therapy
phthalazine derivative: PD, pharmacology
phthalazine derivative: PO, oral drug administration
troxacitabine: CT, clinical trial
troxacitabine: CB, drug combination
troxacitabine: CM, drug comparison
troxacitabine: DT, drug therapy
troxacitabine: PK, pharmacokinetics

troxacitabine: PD, pharmacology
lamivudine: PD, pharmacology
deoxycytidine kinase: EC, endogenous compound
unindexed drug
unclassified drug

RN (imatinib) 152459-95-5, **220127-57-1**; (cytarabine) 147-94-4, 69-74-9; (azacitidine) 320-67-2, 52934-49-3; (5 aza 2' deoxycytidine) 2353-33-5; (etoposide) 33419-42-0; (mitoxantrone) 65271-80-9, 70476-82-3; (protein p21) 85306-28-1; (vasculotropin) 127464-60-2; (bevacizumab) 216974-75-3; (vatalanib) 212141-54-3, 212142-18-2; (n benzoylstaurosporine) 120685-11-2; (semaxanib) 186610-95-7; (**troxacitabine**) **145918-75-8**; (lamivudine) 134678-17-4, 134680-32-3; (deoxycytidine kinase) 9039-45-6

CN **(1) Gleevec; (2) Sti 571**; (3) Avastin; Laq 824; Ptk 787; Pkc 412; Su 5416; Ag 013736

CO (2) Novartis; (3) Genentech

L89 ANSWER 26 OF 54 EMBASE
on STN

ACCESSION NUMBER: 2003396846 EMBASE
TITLE: Phase 2 clinical and pharmacologic study of clofarabine in patients with refractory or relapsed acute leukemia.
AUTHOR: Kantarjian H.; Gandhi V.; Cortes J.; Verstovsek S.; Du M.; Garcia-Manero G.; Giles F.; Faderl S.; O'Brien S.; Jeha S.; Davis J.; Shaked Z.; Craig A.; Keating M.; Plunkett W.; Freireich E.J.
CORPORATE SOURCE: H. Kantarjian, Department of Leukemia, Box 428, Univ. Texas MD Anderson Cancer Ctr., 1515 Holcombe Blvd, Houston, TX 77030, United States. hkantarj@mdanderson.org
SOURCE: Blood, (1 Oct 2003) 102/7 (2379-2386).
Refs: 40
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In a phase 2 study, 62 patients with relapsed and refractory acute myeloid leukemia (AML; n = 31), myelodysplastic syndrome (MDS; n = 8), chronic myeloid leukemia in blastic phase (CMLBP; n = 11), and acute lymphocytic leukemia (ALL; n = 12) received 40 mg/m(2) clofarabine intravenously over 1 hour daily for 5 days, every 3 to 6 weeks. Twenty patients (32%) achieved complete response (CR), 1 had a partial response (PR), and 9 (15%) achieved CR but without platelet recovery (CRp), for an overall response rate of 48%. In AML, responses were noted in 2 (18%) of 11 patients in first salvage with short first CR (≤ 12 months), in 7 (87%) of 8 patients with longer first CR, and in 8 (67%) of 12 patients in second or subsequent salvage. Responses were observed in 4 of 8 patients with high-risk MDS (50%), in 7 (64%) of 11 with CML-BP, and in 2 (17%) of 12 with ALL. Severe reversible liver dysfunction was noted in 15% to 25%. After the first clofarabine infusion, responders accumulated more clofarabine triphosphate in blasts compared with nonresponders (median 18 vs 10 μM; P = .03). This increased only in responders (median, 1.8-fold; P = .008) after the second clofarabine infusion. In summary, clofarabine is active in acute leukemias and MDS; cellular pharmacokinetics may have prognostic significance. .COPYRGT. 2003 by The

American Society of Hematology.
CT Medical Descriptors:
*cancer recurrence
*acute granulocytic leukemia: DT, drug therapy
*myelodysplastic syndrome: DT, drug therapy
*chronic myeloid leukemia: DT, drug therapy
*acute lymphocytic leukemia: DT, drug therapy
thrombocyte count
drug response
salvage therapy
high risk population
disease severity
liver dysfunction: SI, side effect
drug infusion
blast cell
prognosis
drug mechanism
treatment outcome
drug blood level
rash: SI, side effect
hand foot syndrome: SI, side effect
mucosa inflammation: SI, side effect
drug fatality: SI, side effect
diarrhea: SI, side effect
nausea: SI, side effect
vomiting: SI, side effect
drug half life
blood toxicity: SI, side effect
infection: SI, side effect
sepsis: SI, side effect
human
male
female
major clinical study
clinical trial
phase 2 clinical trial
controlled study
aged
adult
article
priority journal
Drug Descriptors:
*nucleoside derivative: AE, adverse drug reaction
*nucleoside derivative: CT, clinical trial
*nucleoside derivative: CR, drug concentration
*nucleoside derivative: DT, drug therapy
*nucleoside derivative: PK, pharmacokinetics
*nucleoside derivative: PD, pharmacology
*nucleoside derivative: IV, intravenous drug administration
*clofarabine: AE, adverse drug reaction
*clofarabine: CT, clinical trial
*clofarabine: CR, drug concentration
*clofarabine: DT, drug therapy
*clofarabine: PK, pharmacokinetics
*clofarabine: PD, pharmacology
*clofarabine: IV, intravenous drug administration
thalidomide: DT, drug therapy
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
cytarabine: CB, drug combination

cytarabine: DT, drug therapy
topotecan: CB, drug combination
topotecan: DT, drug therapy
granulocyte colony stimulating factor: CB, drug combination
granulocyte colony stimulating factor: DT, drug therapy
imatinib: CB, drug combination
imatinib: DT, drug therapy
gemtuzumab ozogamicin: CB, drug combination
gemtuzumab ozogamicin: DT, drug therapy
troxacitabine: CB, drug combination
troxacitabine: DT, drug therapy
prednisone: CB, drug combination
prednisone: DT, drug therapy
vincristine: CB, drug combination
vincristine: DT, drug therapy
daunorubicin: CB, drug combination
daunorubicin: DT, drug therapy
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
dexamethasone: CB, drug combination
dexamethasone: DT, drug therapy
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
alpha interferon: DT, drug therapy
unclassified drug

RN (thalidomide) 50-35-1; (cyclophosphamide) 50-18-0; (cytarabine) 147-94-4, 69-74-9; (topotecan) 119413-54-6, 123948-87-8; (imatinib) 152459-95-5, **220127-57-1**; (**troxacitabine**) **145918-75-8**; (prednisone) 53-03-2; (vincristine) 57-22-7; (daunorubicin) 12707-28-7, 20830-81-3, 23541-50-6; (doxorubicin) 23214-92-8, 25316-40-9; (dexamethasone) 50-02-2; (mitoxantrone) 65271-80-9, 70476-82-3

CO Ash Stevens (United States)

L89 ANSWER 27 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003175598 EMBASE
TITLE: Perspectives on the treatment of chronic phase and advanced phase CML and Philadelphia chromosome positive ALL.
AUTHOR: Schiffer C.A.; Hehlmann R.; Larson R.
CORPORATE SOURCE: C.A. Schiffer, Division of Hematology and Oncology, Karmanos Cancer Institute, Wayne State Univ. School of Medicine, 505 Hudson 3990 John R, Detroit, MI 48201, United States
SOURCE: Leukemia, (1 Apr 2003) 17/4 (691-699).
Refs: 73
ISSN: 0887-6924 CODEN: LEUKED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Chronic myeloid leukaemia (CML) is a malignant disease of the bone marrow characterised by the presence of the Philadelphia (Ph) chromosome. About 20% of acute lymphoblastic leukaemia (ALL) patients also show this genetic abnormality. A new drug, imatinib (**Glivec**.RTM., Novartis Pharma

AG, Basel, Switzerland, and formerly STI571) is having a profound effect on the treatment and management of all stages of CML and Philadelphia chromosome positive (Ph+) ALL. New treatment algorithms are being developed. Should imatinib replace or be combined with existing therapies? To address this question, we review the pros and cons of therapy with interferon-α (IFN-α), allogeneic transplantation, autologous transplantation, imatinib, and in the case of Ph+ ALL, chemotherapy and experimental approaches. Conservative and aggressive treatments will be discussed and new molecular methods of monitoring cytogenetic response and their significance will also be reviewed.

CT Medical Descriptors:
*chronic myeloid leukemia: DR, drug resistance
*chronic myeloid leukemia: DT, drug therapy
*chronic myeloid leukemia: RT, radiotherapy
*chronic myeloid leukemia: TH, therapy
*acute lymphoblastic leukemia: DT, drug therapy
*acute lymphoblastic leukemia: TH, therapy
*Philadelphia 1 chromosome
advanced cancer: DR, drug resistance
advanced cancer: DT, drug therapy
advanced cancer: TH, therapy
bone marrow cancer: DR, drug resistance
bone marrow cancer: DT, drug therapy
bone marrow cancer: RT, radiotherapy
bone marrow cancer: TH, therapy
clinical feature
genetic disorder: DR, drug resistance
genetic disorder: DT, drug therapy
genetic disorder: RT, radiotherapy
genetic disorder: TH, therapy
drug effect
cancer staging
algorithm
allogenic bone marrow transplantation
autologous bone marrow transplantation
cancer combination chemotherapy
conservative treatment
methodology
patient monitoring
cytogenetics
treatment outcome
drug indication
dose response
withdrawal syndrome: SI, side effect
cancer radiotherapy
cancer resistance
diarrhea: SI, side effect
nausea and vomiting: SI, side effect
fluid retention
blood toxicity: SI, side effect
human
clinical trial
article
priority journal
Drug Descriptors:
*imatinib: AE, adverse drug reaction
*imatinib: CT, clinical trial
*imatinib: CB, drug combination
*imatinib: CM, drug comparison
*imatinib: DO, drug dose

*imatinib: DT, drug therapy
*imatinib: PD, pharmacology
alpha interferon: AE, adverse drug reaction
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: CM, drug comparison
alpha interferon: DO, drug dose
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
hydroxyurea: CB, drug combination
hydroxyurea: CM, drug comparison
hydroxyurea: DT, drug therapy
hydroxyurea: PD, pharmacology
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: CB, drug combination
antineoplastic agent: CM, drug comparison
antineoplastic agent: DO, drug dose
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
busulfan: CB, drug combination
busulfan: DT, drug therapy
cytarabine: AE, adverse drug reaction
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
cytarabine: PD, pharmacology
anthracycline: AE, adverse drug reaction
anthracycline: CB, drug combination
anthracycline: DT, drug therapy
anthracycline: PD, pharmacology
cladribine: DO, drug dose
cladribine: DT, drug therapy
cladribine: PD, pharmacology
purine derivative: DO, drug dose
purine derivative: DT, drug therapy
purine derivative: PD, pharmacology
5 aza 2' deoxycytidine: DT, drug therapy
5 aza 2' deoxycytidine: PD, pharmacology
pyrimidine derivative: DT, drug therapy
pyrimidine derivative: PD, pharmacology
troxacitabine: DT, drug therapy
troxacitabine: PD, pharmacology
nucleoside analog: DT, drug therapy
nucleoside analog: PD, pharmacology
antibody conjugate: DT, drug therapy
antibody conjugate: PD, pharmacology
gemtuzumab ozogamicin: CB, drug combination
gemtuzumab ozogamicin: DT, drug therapy
gemtuzumab ozogamicin: PD, pharmacology
protein farnesyltransferase inhibitor: CB, drug combination
protein farnesyltransferase inhibitor: DT, drug therapy
protein farnesyltransferase inhibitor: PD, pharmacology
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
cyclophosphamide: PD, pharmacology
vincristine: CB, drug combination
vincristine: DT, drug therapy

vincristine: PD, pharmacology
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
doxorubicin: PD, pharmacology
dexamethasone: CB, drug combination
dexamethasone: DT, drug therapy
dexamethasone: PD, pharmacology
methotrexate: CB, drug combination
methotrexate: DO, drug dose
methotrexate: DT, drug therapy
methotrexate: PD, pharmacology

RN (imatinib) 152459-95-5, **220127-57-1**; (hydroxyurea) 127-07-1; (busulfan) 55-98-1; (cytarabine) 147-94-4, 69-74-9; (cladribine) 4291-63-8; (5 aza 2' deoxycytidine) 2353-33-5; (**troxacitabine**) **145918-75-8**; (cyclophosphamide) 50-18-0; (vincristine) 57-22-7; (doxorubicin) 23214-92-8, 25316-40-9; (dexamethasone) 50-02-2; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5

CN **(1) Glivec; (2) Sti 571**; (3) Mylotarg

CO (2) Novartis (Switzerland); (3) Wyeth (United States)

L89 ANSWER 28 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003165547 EMBASE
TITLE: New antileukemic agents.
AUTHOR: Mantadakis E.; Kalmanti M.
CORPORATE SOURCE: Dr. M. Kalmanti, Pediatric Hematology/Oncology Clinic, University Hospital of Heraklion, 71 110 Heraklion, Crete, Greece. pedhem@med.uoc.gr
SOURCE: Pediatric Hematology and Oncology, (2003) 20/3 (173-185). Refs: 70
ISSN: 0888-0018 CODEN: PHONEN
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Despite the tremendous progress in the treatment of childhood leukemias over the last 50 years, certain subgroups of children continue to have poor prognosis. Hence, there is a need for development of new antileukemic agents. In this review, the authors describe results of clinical trials of several new antileukemic compound with different mechanisms of action (signal transduction inhibitors, nucleoside analogs, DNA hypomethylators, angiogenesis inhibitors, and monoclonal antibodies). Although most of these compounds are not used in pediatric leukemias, the concepts surrounding their clinical development are important to all pediatric hematologists/oncologists.

CT Medical Descriptors:
*childhood leukemia: DR, drug resistance
*childhood leukemia: DT, drug therapy
*childhood leukemia: TH, therapy
*cancer chemotherapy
prognosis
drug mechanism
signal transduction
DNA methylation
treatment outcome

chronic myeloid leukemia: DT, drug therapy
malignant transformation
antineoplastic activity
acute lymphoblastic leukemia: DT, drug therapy
hematopoietic stem cell transplantation
blood toxicity: SI, side effect
liver dysfunction: SI, side effect
gene mutation
oncogene ras
side effect: SI, side effect
drug efficacy
stomatitis: SI, side effect
hand foot syndrome: SI, side effect
skin manifestation: SI, side effect
desquamation: SI, side effect
pruritus: SI, side effect
bone marrow suppression: SI, side effect
drug eruption: SI, side effect
drug half life
drug clearance
drug blood level
drug solubility
neurotoxicity: SI, side effect
pancytopenia: SI, side effect
anemia: SI, side effect
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
liver toxicity: SI, side effect
mucosa inflammation: SI, side effect
hyperbilirubinemia: SI, side effect
human
clinical trial
review
Drug Descriptors:
*antileukemic agent: AE, adverse drug reaction
*antileukemic agent: CT, clinical trial
*antileukemic agent: CR, drug concentration
*antileukemic agent: DO, drug dose
*antileukemic agent: DT, drug therapy
*antileukemic agent: PR, pharmaceutics
*antileukemic agent: PK, pharmacokinetics
*antileukemic agent: PD, pharmacology
*antileukemic agent: IV, intravenous drug administration
nucleoside derivative: AE, adverse drug reaction
nucleoside derivative: CT, clinical trial
nucleoside derivative: CR, drug concentration
nucleoside derivative: DO, drug dose
nucleoside derivative: DT, drug therapy
nucleoside derivative: PR, pharmaceutics
nucleoside derivative: PK, pharmacokinetics
nucleoside derivative: PD, pharmacology
nucleoside derivative: IV, intravenous drug administration
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DT, drug therapy
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD,

pharmacology
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
monoclonal antibody: AE, adverse drug reaction
monoclonal antibody: CT, clinical trial
monoclonal antibody: CB, drug combination
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
monoclonal antibody: IV, intravenous drug administration
aletuzumab: AE, adverse drug reaction
aletuzumab: CT, clinical trial
aletuzumab: DT, drug therapy
aletuzumab: PD, pharmacology
aletuzumab: IV, intravenous drug administration
gemtuzumab ozogamicin: AE, adverse drug reaction
gemtuzumab ozogamicin: CT, clinical trial
gemtuzumab ozogamicin: DT, drug therapy
gemtuzumab ozogamicin: PD, pharmacology
protein kinase inhibitor: AE, adverse drug reaction
protein kinase inhibitor: CT, clinical trial
protein kinase inhibitor: DO, drug dose
protein kinase inhibitor: DT, drug therapy
protein kinase inhibitor: PD, pharmacology
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PD, pharmacology
pyrrole derivative: PD, pharmacology
imatinib: AE, adverse drug reaction
imatinib: CT, clinical trial
imatinib: DO, drug dose
imatinib: DT, drug therapy
imatinib: PD, pharmacology
interferon: DT, drug therapy
Flt3 ligand: EC, endogenous compound
n benzoylstaurosporine: PD, pharmacology
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: DT, drug therapy
protein farnesyltransferase inhibitor: PD, pharmacology
protein farnesyltransferase inhibitor: PO, oral drug administration
r 115777: CT, clinical trial
r 115777: DT, drug therapy
r 115777: PD, pharmacology
r 115777: PO, oral drug administration
troxacitabine: AE, adverse drug reaction
troxacitabine: CB, drug combination
troxacitabine: CM, drug comparison
troxacitabine: CR, drug concentration
troxacitabine: DO, drug dose
troxacitabine: DT, drug therapy
fludarabine: DT, drug therapy
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
nelarabine: AE, adverse drug reaction
nelarabine: CT, clinical trial
nelarabine: CM, drug comparison
nelarabine: PR, pharmaceutics
nelarabine: PK, pharmacokinetics

nelarabine: PD, pharmacology
nelarabine: IV, intravenous drug administration
guanine arabinoside: CM, drug comparison
guanine arabinoside: CR, drug concentration
5 aza 2' deoxycytidine: AE, adverse drug reaction
5 aza 2' deoxycytidine: CT, clinical trial
5 aza 2' deoxycytidine: DT, drug therapy
5 aza 2' deoxycytidine: PD, pharmacology
unclassified drug
zarnestra
semixanib
pk 1166
pkc 412
506u78

RN (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine) 212142-18-2; (imatinib) 152459-95-5, **220127-57-1**; (Flt3 ligand) 171404-15-2; (n benzoylstaurosporine) 120685-11-2; (**troxacitabine**) **145918-75-8**; (fludarabine) 21679-14-1; (cytarabine) 147-94-4, 69-74-9; (guanine arabinoside) 38819-10-2; (5 aza 2' deoxycytidine) 2353-33-5

CN (1) R 115777; (2) Zarnestra; (3) Su 5416; (4) Semixanib; Pk 1166; Ptk 787; Zk 222584; St 1571; Pkc 412; **Bch 4556**; 506u78; Su 6668

CO (2) Janssen Ortho; (4) Sugen (United States)

L89 ANSWER 29 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002047444 EMBASE

TITLE: Phase II study of **troxacitabine**, a novel dioxolane nucleoside analog, in patients with refractory leukemia.

AUTHOR: Giles F.J.; Garcia-Manero G.; Cortes J.E.; Baker S.D.; Miller C.B.; O'Brien S.M.; Thomas D.A.; Andreeff M.; Bivins C.; Jolivet J.; Kantarjian H.M.

CORPORATE SOURCE: Dr. F.J. Giles, University of Texas, M.D. Anderson Cancer Center, Department of Leukemia, 1400 Holcombe Blvd, Houston, TX 77030, United States. fgiles@mdanderson.org

SOURCE: Journal of Clinical Oncology, (1 Feb 2002) 20/3 (656-664). Refs: 43
ISSN: 0732-183X CODEN: JCONDN

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Purpose: To investigate the activity of a novel dioxolane L-nucleoside analog, **troxacitabine** (L-(-)-OddC, **BCH-4556**), in patients with refractory leukemia. Patients and Methods: Study participants were patients with refractory or relapsed acute myeloid (AML) or lymphocytic (ALL) leukemia, myelodysplastic syndromes (MDS), or chronic myelogenous leukemia in blastic phase (CML-BP). **Troxacitabine** was provided as an intravenous infusion for more than 30 minutes daily for 5 days at a dose of 8.0 mg/m(2)/d (40 mg/m(2) per course). Courses were given every 3 to 4 weeks according to antileukemic efficacy. Results: Forty-two patients (AML, 18 patients; MDS, one patient; ALL, six patients;

CML-BP, 17 patients) were treated. Median age was 51 years (range, 23 to 80 years); 22 patients were male. Stomatitis was the most significant adverse event, with three patients (7%) and two patients (5%), respectively, experiencing grade 3 or 4 toxicity. Ten patients (24%) had grade 3 hand-foot syndrome, and two patients (5%) had grade 3 skin rash. One patient (2%) had grade 3 fatigue and anorexia. Marrow hypoplasia occurred between days 14 and 28 in 12 (75%) of 16 assessable patients with AML. Two complete remissions and one partial remission (18%) were observed in 16 assessable patients with AML. None of six patients with ALL responded. Six (37%) of 16 assessable patients with CML-BP experienced a return to chronic-phase disease. Conclusion: **Troxacitabine** has significant antileukemic activity in patients with AML and CML-BP.

CT Medical Descriptors:
*leukemia: DT, drug therapy
*cancer recurrence: DT, drug therapy
acute granulocytic leukemia: DT, drug therapy
lymphatic leukemia: DT, drug therapy
myelodysplastic syndrome: DT, drug therapy
chronic myeloid leukemia: DT, drug therapy
blast cell crisis: DT, drug therapy
drug efficacy
antineoplastic activity
stomatitis: SI, side effect
hand foot syndrome: SI, side effect
rash: SI, side effect
fatigue: SI, side effect
anorexia: SI, side effect
bone marrow hypoplasia: SI, side effect
disease severity
cancer regression
chronic disease
area under the curve
human
male
female
clinical article
clinical trial
phase 2 clinical trial
aged
adult
article
priority journal
Drug Descriptors:
***troxacitabine: AE, adverse drug reaction**
***troxacitabine: CT, clinical trial**
***troxacitabine: AN, drug analysis**
***troxacitabine: CR, drug concentration**
***troxacitabine: DO, drug dose**
***troxacitabine: DT, drug therapy**
***troxacitabine: PK, pharmacokinetics**
***troxacitabine: IV, intravenous drug administration**
*1,3 dioxolane derivative: AE, adverse drug reaction
*1,3 dioxolane derivative: CT, clinical trial
*1,3 dioxolane derivative: AN, drug analysis
*1,3 dioxolane derivative: CR, drug concentration
*1,3 dioxolane derivative: DO, drug dose
*1,3 dioxolane derivative: DT, drug therapy
*1,3 dioxolane derivative: PK, pharmacokinetics
*1,3 dioxolane derivative: IV, intravenous drug administration

*nucleoside analog: AE, adverse drug reaction
*nucleoside analog: CT, clinical trial
*nucleoside analog: AN, drug analysis
*nucleoside analog: CR, drug concentration
*nucleoside analog: DO, drug dose
*nucleoside analog: DT, drug therapy
*nucleoside analog: PK, pharmacokinetics
*nucleoside analog: IV, intravenous drug administration
deoxycytidine: AN, drug analysis
cytarabine: AN, drug analysis
fludarabine: AN, drug analysis
cladribine
cyclophosphamide
topotecan
tioguanine
daunorubicin
mitoxantrone
imatinib
idarubicin
etoposide
vincristine
dexamethasone
clofarabine
5 aza 2' deoxycytidine
hydroxyurea
busulfan
homoharringtonine
thymocyte antibody
tallimustine
methotrexate
alpha interferon
unclassified drug

RN (**troxacitabine**) **145918-75-8**; (deoxycytidine) 951-77-9; (cytarabine) 147-94-4, 69-74-9; (fludarabine) 21679-14-1; (cladribine) 4291-63-8; (cyclophosphamide) 50-18-0; (topotecan) 119413-54-6, 123948-87-8; (tioguanine) 154-42-7; (daunorubicin) 12707-28-7, 20830-81-3, 23541-50-6; (mitoxantrone) 65271-80-9, 70476-82-3; (imatinib) 152459-95-5, **220127-57-1**; (idarubicin) 57852-57-0, 58957-92-9; (etoposide) 33419-42-0; (vincristine) 57-22-7; (dexamethasone) 50-02-2; (5 aza 2' deoxycytidine) 2353-33-5; (hydroxyurea) 127-07-1; (busulfan) 55-98-1; (homoharringtonine) 26833-87-4; (tallimustine) 115308-98-0; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5

CN **(1) Bch 4556; Sti 571**

CO (1) Suire biochem (Canada)

L89 ANSWER 30 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002227269 EMBASE

TITLE: **Troxacitabine**-based therapy of refractory leukemia.

AUTHOR: Giles F.J.

CORPORATE SOURCE: Dr. F.J. Giles, Section of Develop. Therapeutics, Univ. of TX M.D. Anderson Cancer Ctr, Department of Leukemia, 1515 Holcombe Boulevard, Houston, TX 77030-4095, United States. fgiles@mdanderson.org

SOURCE: Expert Review of Anticancer Therapy, (2002) 2/3 (261-266). Refs: 38
ISSN: 1473-7140 CODEN: ERATBJ

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Unique among currently approved or in-development nucleoside analogs, **troxacitabine** (**Troxatyl**.RTM.) is an L-nucleoside with significant cytotoxic activity. Its stereochemistry and cellular transport characteristics render it insensitive to some tumor cell mechanisms of resistance to D-nucleosides, such as cytarabine and fludarabine. **Troxacitabine**'s dose-limiting toxicities were mucositis and hand-foot syndrome in patients with refractory leukemia. Three complete and one partial remissions were observed in 30 patients with refractory acute myeloid leukemia on a Phase I study. Significant activity in blastic phase of chronic myeloid leukemia was seen on a Phase II study. Combinations of **troxacitabine** with ara-C, topotecan and idarubicin are active in patients with refractory acute myeloid leukemia (AML). Phase II studies in patients with refractory lymphoproliferative diseases are ongoing. **Troxacitabine** merits further study in patients with hematological malignancies.

CT Medical Descriptors:
*acute granulocytic leukemia: DT, drug therapy
*acute granulocytic leukemia: TH, therapy
cytotoxicity
drug activity
stereochemistry
cell transport
sensitivity analysis
tumor cell
cell activity
drug response
mucosa inflammation: SI, side effect
hand foot syndrome: DT, drug therapy
hand foot syndrome: SI, side effect
cancer regression
lymphoproliferative disease: DT, drug therapy
hematologic disease
prostate cancer: DT, drug therapy
stem cell transplantation
rash: DT, drug therapy
rash: SI, side effect
drug blood level
fatigue: SI, side effect
gastrointestinal symptom: SI, side effect
bone marrow hypoplasia: SI, side effect
liver disease: SI, side effect
hyperbilirubinemia: SI, side effect
drug efficacy
human
clinical trial
controlled study
adult
article
Drug Descriptors:
***troxacitabine: AE, adverse drug reaction**
***troxacitabine: CT, clinical trial**
***troxacitabine: AN, drug analysis**
***troxacitabine: CB, drug combination**

***troxacitabine: CM, drug comparison**
***troxacitabine: CR, drug concentration**
***troxacitabine: DO, drug dose**
***troxacitabine: DT, drug therapy**
***troxacitabine: PK, pharmacokinetics**
***troxacitabine: PD, pharmacology**
***troxacitabine: IV, intravenous drug administration**
cytarabine: AE, adverse drug reaction
cytarabine: CT, clinical trial
cytarabine: AN, drug analysis
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
cytarabine: PK, pharmacokinetics
cytarabine: PD, pharmacology
cytarabine: IV, intravenous drug administration
fludarabine: AN, drug analysis
fludarabine: CM, drug comparison
fludarabine: PK, pharmacokinetics
fludarabine: PD, pharmacology
topotecan: AE, adverse drug reaction
topotecan: CT, clinical trial
topotecan: AN, drug analysis
topotecan: CB, drug combination
topotecan: DO, drug dose
topotecan: DT, drug therapy
topotecan: PK, pharmacokinetics
topotecan: PD, pharmacology
topotecan: IV, intravenous drug administration
idarubicin: AE, adverse drug reaction
idarubicin: CT, clinical trial
idarubicin: AN, drug analysis
idarubicin: CB, drug combination
idarubicin: CM, drug comparison
idarubicin: DO, drug dose
idarubicin: DT, drug therapy
idarubicin: PK, pharmacokinetics
idarubicin: PD, pharmacology
idarubicin: IV, intravenous drug administration
5 aza 2' deoxycytidine: AN, drug analysis
5 aza 2' deoxycytidine: CM, drug comparison
5 aza 2' deoxycytidine: DV, drug development
5 aza 2' deoxycytidine: PK, pharmacokinetics
5 aza 2' deoxycytidine: PD, pharmacology
506 u78: AN, drug analysis
506 u78: CM, drug comparison
506 u78: DV, drug development
506 u78: PD, pharmacology
clofarabine: AN, drug analysis
clofarabine: CM, drug comparison
clofarabine: DV, drug development
clofarabine: PD, pharmacology
nucleoside derivative: AE, adverse drug reaction
nucleoside derivative: CT, clinical trial
nucleoside derivative: AN, drug analysis
nucleoside derivative: CM, drug comparison
nucleoside derivative: DV, drug development
nucleoside derivative: DT, drug therapy
nucleoside derivative: PK, pharmacokinetics

nucleoside derivative: PD, pharmacology
lamivudine: PD, pharmacology
deoxycytidine: AN, drug analysis
deoxycytidine: CM, drug comparison
deoxycytidine: PK, pharmacokinetics
deoxycytidine: PD, pharmacology
prednisone: DT, drug therapy
prednisone: PD, pharmacology
prednisone: PO, oral drug administration
pyridoxine: DT, drug therapy
pyridoxine: PD, pharmacology
dimethyl sulfoxide: DT, drug therapy
dimethyl sulfoxide: PD, pharmacology
dimethyl sulfoxide: TP, topical drug administration
imatinib: PD, pharmacology
unclassified drug

RN (**troxacitabine**) **145918-75-8**; (cytarabine) 147-94-4, 69-74-9; (fludarabine) 21679-14-1; (topotecan) 119413-54-6, 123948-87-8; (idarubicin) 57852-57-0, 58957-92-9; (5 aza 2' deoxycytidine) 2353-33-5; (lamivudine) 134678-17-4, 134680-32-3; (deoxycytidine) 951-77-9; (prednisone) 53-03-2; (pyridoxine) 12001-77-3, 58-56-0, 65-23-6, 8059-24-3; (dimethyl sulfoxide) 67-68-5; (imatinib) 152459-95-5, **220127-57-1**

CN **(1) Troxatyl**

CO (1) Shire (Canada)

L89 ANSWER 31 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002367914 EMBASE

TITLE: **Troxacitabine** activity in extramedullary myeloid leukemia.

AUTHOR: Alvarado Y.Yesid; Kantarjian H.M.; Cortes J.E.; Apostolidou E.; Bivins C.; Giles F.J.

CORPORATE SOURCE: F.J. Giles, Department of Leukemia, M.D. Anderson Cancer Center, The University of Texas, 1400 Holcombe Boulevard, Houston, TX 77030, United States. frankgiles@aol.com

SOURCE: Hematology, (2002) 7/3 (179-185).
Refs: 36
ISSN: 1024-5340 CODEN: HMATFL

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB **Troxacitabine** is a novel L-enantiomer nucleoside analog with unique properties in terms of its structure, pharmacokinetics, intracellular transport, and susceptibility to mechanisms of resistance. **Troxacitabine** has significant activity in patients with refractory myeloid leukemias, both as a single agent and when combined with standard anti-leukemia agents. In a cohort of 170 patients with refractory myeloid leukemia treated with **troxacitabine**-based regimens on Phase 1 or 2 studies, 10 (6%) had biopsy-proven extramedullary disease, either with or without bone marrow involvement. Six of these patients who received single-agent **troxacitabine**, 4 received a combination of **troxacitabine** and cytarabine. Complete response and disappearance of all extramedullary lesions were observed in 6 (60%) of these 10 patients. Two of the 6 responding patients relapsed within 3 months, 2

patients had remissions of 8 and 9 months duration, respectively, 1 patient is in on-going remission at 3, and 1 patient is lost to follow-up. **Troxacitabine**-based therapy had significant antileukemic activity in extramedullary myeloid leukemias and warrants further investigation in this clinical situation.

CT Medical Descriptors:
*myeloid leukemia: DI, diagnosis
*myeloid leukemia: DR, drug resistance
*myeloid leukemia: DT, drug therapy
*myeloid leukemia: RT, radiotherapy
*myeloid leukemia: TH, therapy
enantiomer
drug structure
drug transport
cohort analysis
biopsy
bone marrow
drug response
cancer recurrence
leukemia remission
disease duration
follow up
allogenic bone marrow transplantation
drug half life
treatment failure
mucosa inflammation: SI, side effect
hand foot syndrome: SI, side effect
rash: SI, side effect
human
male
female
major clinical study
clinical trial
phase 1 clinical trial
phase 2 clinical trial
controlled study
human tissue
aged
adult
article
priority journal
Drug Descriptors:
***troxacitabine: AE, adverse drug reaction**
***troxacitabine: CT, clinical trial**
***troxacitabine: AN, drug analysis**
***troxacitabine: CB, drug combination**
***troxacitabine: CM, drug comparison**
***troxacitabine: DT, drug therapy**
***troxacitabine: PK, pharmacokinetics**
***troxacitabine: PD, pharmacology**
***troxacitabine: IV, intravenous drug administration**
nucleoside analog: AE, adverse drug reaction
nucleoside analog: CT, clinical trial
nucleoside analog: AN, drug analysis
nucleoside analog: CB, drug combination
nucleoside analog: CM, drug comparison
nucleoside analog: DT, drug therapy
nucleoside analog: PK, pharmacokinetics
nucleoside analog: PD, pharmacology
nucleoside analog: IV, intravenous drug administration

antileukemic agent: AE, adverse drug reaction
antileukemic agent: CT, clinical trial
antileukemic agent: AN, drug analysis
antileukemic agent: CB, drug combination
antileukemic agent: CM, drug comparison
antileukemic agent: DT, drug therapy
antileukemic agent: PK, pharmacokinetics
antileukemic agent: PD, pharmacology
antileukemic agent: TL, intrathecal drug administration
antileukemic agent: IV, intravenous drug administration
cytarabine: AN, drug analysis
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
cytarabine: TL, intrathecal drug administration
cytarabine: IV, intravenous drug administration
idarubicin: CB, drug combination
idarubicin: DT, drug therapy
idarubicin: IV, intravenous drug administration
topotecan: CB, drug combination
topotecan: DT, drug therapy
topotecan: IV, intravenous drug administration
hydroxyurea: CB, drug combination
hydroxyurea: DT, drug therapy
interferon: CB, drug combination
interferon: DT, drug therapy
imatinib: CB, drug combination
imatinib: DT, drug therapy
busulfan: CB, drug combination
busulfan: DT, drug therapy
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
fludarabine: AN, drug analysis
fludarabine: CB, drug combination
fludarabine: DT, drug therapy
melphalan: CB, drug combination
melphalan: DT, drug therapy
5 aza 2' deoxycytidine: CB, drug combination
5 aza 2' deoxycytidine: DT, drug therapy
homoharringtonine: CB, drug combination
homoharringtonine: DT, drug therapy
monoclonal antibody: CB, drug combination
monoclonal antibody: DT, drug therapy
arsenic trioxide: CB, drug combination
arsenic trioxide: DT, drug therapy
methotrexate: CB, drug combination
methotrexate: DT, drug therapy
gemcitabine: AN, drug analysis

RN (**troxacitabine**) **145918-75-8**; (cytarabine) 147-94-4, 69-74-9; (idarubicin) 57852-57-0, 58957-92-9; (topotecan) 119413-54-6, 123948-87-8; (hydroxyurea) 127-07-1; (imatinib) 152459-95-5, **220127-57-1**; (busulfan) 55-98-1; (cyclophosphamide) 50-18-0; (fludarabine) 21679-14-1; (melphalan) 148-82-3; (5 aza 2' deoxycytidine) 2353-33-5; (homoharringtonine) 26833-87-4; (arsenic trioxide) 1303-24-8, 1327-53-3, 13464-58-9, 15502-74-6; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (gemcitabine) 103882-84-4

CN **Gleevec; Sti 571**

CO Shire (Canada)

L89 ANSWER 32 OF 54 EMBASE

on STN
ACCESSION NUMBER: 2002369569 EMBASE
TITLE: **STI-571** in chronic myelogenous leukaemia.
AUTHOR: Tsao A.S.; Kantarjian H.; Talpaz M.
CORPORATE SOURCE: M. Talpaz, Department of Bioimmunotherapy, MD Anderson Cancer Center, Box 422, 1515 Holcombe Blvd., Houston, TX 77030, United States. mtalpaz@mdanderson.org
SOURCE: British Journal of Haematology, (2002) 119/1 (15-24). Refs: 72
ISSN: 0007-1048 CODEN: BJHEAL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
CT Medical Descriptors:
*chronic myeloid leukemia: DT, drug therapy
*chronic myeloid leukemia: SI, side effect
*chronic myeloid leukemia: TH, therapy
clinical feature
disease course
survival time
pathogenesis
cancer radiotherapy
cancer chemotherapy
cancer survival
protein phosphorylation
antineoplastic activity
drug absorption
drug half life
cancer regression
drug efficacy
drug mechanism
apoptosis
cancer cell culture
point mutation
side effect: SI, side effect
nausea: SI, side effect
muscle cramp: SI, side effect
arthralgia: SI, side effect
myalgia: SI, side effect
edema: SI, side effect
rash: SI, side effect
bone marrow suppression: SI, side effect
diarrhea: SI, side effect
liver toxicity: SI, side effect
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
allogenic bone marrow transplantation
human
nonhuman
clinical trial
article
priority journal
Drug Descriptors:
*imatinib: AE, adverse drug reaction

*imatinib: CT, clinical trial
*imatinib: CB, drug combination
*imatinib: CM, drug comparison
*imatinib: DO, drug dose
*imatinib: DT, drug therapy
*imatinib: PK, pharmacokinetics
*imatinib: PD, pharmacology
*imatinib: PO, oral drug administration
busulfan: AE, adverse drug reaction
busulfan: CB, drug combination
busulfan: DT, drug therapy
busulfan: PD, pharmacology
hydroxyurea: DT, drug therapy
hydroxyurea: PD, pharmacology
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
cyclophosphamide: PD, pharmacology
alpha interferon: AE, adverse drug reaction
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: CM, drug comparison
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: DT, drug therapy
cytarabine: PD, pharmacology
BCR ABL protein: EC, endogenous compound
homoharringtonine: DT, drug therapy
5 aza 2' deoxycytidine: DT, drug therapy
troxacitabine: DT, drug therapy
orosomucoid: EC, endogenous compound
verapamil: DT, drug therapy
verapamil: PD, pharmacology
leptomycin B: CB, drug combination
leptomycin B: DT, drug therapy
leptomycin B: PD, pharmacology

RN (imatinib) 152459-95-5, **220127-57-1**; (busulfan) 55-98-1; (hydroxyurea) 127-07-1; (cyclophosphamide) 50-18-0; (cytarabine) 147-94-4, 69-74-9; (homoharringtonine) 26833-87-4; (5 aza 2' deoxycytidine) 2353-33-5; (**troxacitabine**) **145918-75-8**; (orosomucoid) 79921-18-9; (verapamil) 152-11-4, 52-53-9; (leptomycin B) 87081-35-4

CN **Sti 571; Glivec; Cgp 57148b; Gleevec**

L89 ANSWER 33 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002320865 EMBASE
TITLE: Chronic myeloid leukemia: Current therapies and the potential role of farnesyltransferase inhibitors.
AUTHOR: Keating A.
CORPORATE SOURCE: Dr. A. Keating, Princess Margaret Hospital, 610 University Ave, Toronto, Ont. M5G 2M9, Canada
SOURCE: Seminars in Hematology, (2002) 39/3 SUPPL. 2 (11-17).
Refs: 59
ISSN: 0037-1963 CODEN: SEHEA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The treatment of patients with chronic myeloid leukemia (CML) is evolving rapidly. With conventional chemotherapy the clinical course is characterized by a chronic phase (median duration, 4 to 5 years), followed by an accelerated phase with transition to a terminal blast crisis. Treatment with busulfan or hydroxyurea does not alter the natural history. Interferon alfa (IFN-α) prolongs life expectancy by approximately 20 months but is associated with significant toxicity. Evidence indicates that bone marrow transplantation from a related human leukocyte antigen (HLA)-identical donor can be curative in younger patients. However, transplantation is available to only a minority of patients and entails severe toxicity and transplant-related mortality. Dramatic advances in the understanding of the molecular pathophysiology of CML have led to a new era of targeted therapy. The specific **tyrosine kinase** inhibitor **imatinib mesylate** demonstrates a high level of efficacy in CML with acceptable toxicity. Farnesyltransferase inhibitors (FTIs) are another important class of targeted agents with the potential to act at multiple sites within dysregulated signal transduction networks. ZARNESTRA® (formerly R115777, Ortho Biotech Oncology, Raritan, NJ), an oral FTI, has shown activity and is well tolerated in both chronic- and accelerated-phase patients. With their mechanistic specificity, the new modalities offer the promise of increased antileukemic activity and an improved therapeutic index.
CT Medical Descriptors:
*chronic myeloid leukemia: DT, drug therapy
*chronic myeloid leukemia: TH, therapy
disease course
blast cell crisis
life expectancy
cancer survival
bone marrow transplantation
drug efficacy
drug tolerability
treatment outcome
bone marrow suppression: SI, side effect
diarrhea: SI, side effect
nausea: SI, side effect
vomiting: SI, side effect
headache: SI, side effect
fatigue: SI, side effect
tachycardia: SI, side effect
human
clinical trial
article
priority journal
Drug Descriptors:
*protein farnesyltransferase inhibitor: CT, clinical trial
*protein farnesyltransferase inhibitor: DT, drug therapy
*protein farnesyltransferase inhibitor: PO, oral drug administration
*r 115777: CT, clinical trial
*r 115777: DT, drug therapy
*r 115777: PO, oral drug administration
busulfan: DT, drug therapy
hydroxyurea: DT, drug therapy
recombinant alpha2b interferon: AE, adverse drug reaction
recombinant alpha2b interferon: CT, clinical trial
recombinant alpha2b interferon: DT, drug therapy

protein tyrosine kinase inhibitor: DT, drug therapy
imatinib: AE, adverse drug reaction
imatinib: DT, drug therapy
cytarabine: DT, drug therapy
homoharringtonine: AE, adverse drug reaction
homoharringtonine: DV, drug development
homoharringtonine: DT, drug therapy
5 aza 2' deoxycytidine: DT, drug therapy
troxacitabine: CT, clinical trial
troxacitabine: DT, drug therapy
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: IV, intravenous drug administration
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: CT, clinical trial
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: DT, drug therapy
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: PO, oral drug administration
zarnestra

RN (busulfan) 55-98-1; (hydroxyurea) 127-07-1; (recombinant alpha2b interferon) 98530-12-2; (imatinib) 152459-95-5, **220127-57-1**; (cytarabine) 147-94-4, 69-74-9; (homoharringtonine) 26833-87-4; (5 aza 2' deoxycytidine) 2353-33-5; (**troxacitabine**) **145918-75-8**; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide) 193275-84-2

CN (1) Zarnestra; (2) Myleran; (3) Hydrea; (4) Intron A; (5) Cytosar u; **(6) Gleevec**; (7) Decitabine; **(8) Bch 4556**; (9) Bms 214662; (10) Sch 66336

CO (1) Ortho (United States); (2) Glaxo SmithKline (United States); (4) Schering Corporation (United States); (5) Bedford (United States); (6) Novartis (United States); (7) Supergen (United States); (8) Biochem Corporation (Canada); (9) Bristol Myers Squibb (United States); (10) Schering Plough (United States)

L89 ANSWER 34 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002320864 EMBASE
TITLE: Treatment of acute myeloid leukemia: State-of-the-art and future directions.
AUTHOR: Stone R.M.
CORPORATE SOURCE: Dr. R.M. Stone, Dana-Farber Cancer Institute, 44 Binney St, Boston, MA 02115, United States
SOURCE: Seminars in Hematology, (2002) 39/3 SUPPL. 2 (4-10). Refs: 66
ISSN: 0037-1963 CODEN: SEHEA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Despite major recent advances in the understanding of the molecular biology of the disease, the treatment of acute myeloid leukemia (AML) in adults remains challenging. For the 75% of AML patients older than 60 years, currently available treatments produce significant toxicity with poor overall response rates and survival. In younger patients, standard regimens using cytarabine and an anthracycline for induction followed by some form of intensive postremission therapy can produce response rates of 70%, with 5-year relapse-free survival rates of 25% to 40%. Chromosomal analyses define three prognostic categories with favorable, intermediate, and unfavorable risk. In older adults, AML appears to be an intrinsically resistant disorder of proximal pluripotent hematopoietic stem cells. A variety of targeted therapies currently in development Include modulators of MDR1-mediated drug resistance, immunotherapeutics, angiogenesis inhibitors, proapoptotic antisense oligonucleotides, and specific small molecule inhibitors of **tyrosine kinase** and farnesyltransferase. For example, oral farnesyltransferase inhibitors have demonstrated activity and tolerability in patients with refractory AML and are now in phase II testing. Such targeted therapeutics offer the promise of novel antileukemic activity combined with an improved therapeutic index.
CT Medical Descriptors:
*acute granulocytic leukemia: DT, drug therapy
treatment outcome
cancer survival
age
cancer regression
cancer recurrence
drug response
chromosome analysis
prognosis
hematopoietic stem cell
cancer combination chemotherapy
immunotherapy
multidrug resistance
stomatitis: SI, side effect
bone marrow suppression: SI, side effect
infection: SI, side effect
bleeding: SI, side effect
mucosa inflammation: SI, side effect
nausea: SI, side effect
vomiting: SI, side effect
cardiotoxicity: SI, side effect
human
clinical trial
article
priority journal
Drug Descriptors:
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: DT, drug therapy
anthracycline: CB, drug combination
anthracycline: DT, drug therapy
angiogenesis inhibitor: DV, drug development
angiogenesis inhibitor: DT, drug therapy
antisense oligonucleotide: DV, drug development
antisense oligonucleotide: DT, drug therapy
protein tyrosine kinase inhibitor: DV, drug development

protein tyrosine kinase inhibitor: DT, drug therapy
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: DV, drug development
protein farnesyltransferase inhibitor: DT, drug therapy
protein farnesyltransferase inhibitor: PD, pharmacology
protein farnesyltransferase inhibitor: PO, oral drug administration
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: DT, drug therapy
cladribine: DT, drug therapy
granulocyte colony stimulating factor: CT, clinical trial
granulocyte colony stimulating factor: DT, drug therapy
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: DT, drug therapy
diaziquone: CB, drug combination
diaziquone: DT, drug therapy
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
topotecan: CB, drug combination
topotecan: DT, drug therapy
troxacitabine: AE, adverse drug reaction
troxacitabine: CT, clinical trial
troxacitabine: DT, drug therapy
idarubicin: CB, drug combination
idarubicin: DT, drug therapy
cyclosporin: CT, clinical trial
cyclosporin: CB, drug combination
cyclosporin: DT, drug therapy
valspodar: CT, clinical trial
valspodar: CB, drug combination
valspodar: DT, drug therapy
daunorubicin: CT, clinical trial
daunorubicin: CB, drug combination
daunorubicin: DT, drug therapy
granulocyte macrophage colony stimulating factor: CT, clinical trial
granulocyte macrophage colony stimulating factor: DT, drug therapy
gemtuzumab ozogamicin: DT, drug therapy
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: IV, intravenous drug administration
zarnestra

RN (cytarabine) 147-94-4, 69-74-9; (cladribine) 4291-63-8; (cyclophosphamide) 50-18-0; (etoposide) 33419-42-0; (diaziquone) 57998-68-2; (mitoxantrone) 65271-80-9, 70476-82-3; (topotecan) 119413-54-6, 123948-87-8; (**troxacitabine**) **145918-75-8**; (idarubicin) 57852-57-0, 58957-92-9; (cyclosporin) 79217-60-0; (valspodar) 121584-18-7; (daunorubicin) 12707-28-7, 20830-81-3, 23541-50-6; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8
CN (1) Bms 214662; Zarnestra; Psc 833
CO (1) Schering Plough (United States)

L89 ANSWER 35 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002320863 EMBASE
TITLE: Assessing the future landscape in myeloid malignancies: Evolving insights on farnesyltransferase inhibitors: Introduction.
AUTHOR: Rosenblatt J.D.; Rowe J.M.
CORPORATE SOURCE: Dr. J.D. Rosenblatt, Hematology-Oncology Division, University of Miami, Sylvester Compreh. Cancer Center, 1475 NW 12th Ave, Miami, FL 33136, United States
SOURCE: Seminars in Hematology, (2002) 39/3 SUPPL. 2 (1-3). Refs: 1
ISSN: 0037-1963 CODEN: SEHEA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
CT Medical Descriptors:
*leukemia: DT, drug therapy
acute granulocytic leukemia: DT, drug therapy
chronic myeloid leukemia: DT, drug therapy
myelodysplastic syndrome: DT, drug therapy
treatment planning
treatment outcome
human
clinical trial
editorial
priority journal
Drug Descriptors:
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: DT, drug therapy
retinoic acid: DT, drug therapy
imatinib: DT, drug therapy
r 115777: CT, clinical trial
r 115777: DT, drug therapy
topotecan: DT, drug therapy
troxacitabine: DT, drug therapy
valspodar: DT, drug therapy
1 [4 (11,11 difluorodibenzo[b,e]bicyclo[5.1.0]oct 5 yl) 1 piperazinyl] 3 (5 quinolinyloxy) 2 propanol: DT, drug therapy
g 3139: DT, drug therapy
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: DT, drug therapy
zarnestra
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine
RN (retinoic acid) 302-79-4; (imatinib) 152459-95-5, **220127-57-1**; (topotecan) 119413-54-6, 123948-87-8; (**troxacitabine**) **145918-75-8**; (valspodar) 121584-18-7; (1 [4 (11,11 difluorodibenzo[b,e]bicyclo[5.1.0]oct 5 yl) 1 piperazinyl] 3 (5 quinolinyloxy) 2 propanol) 167465-36-3; (g 3139) 190977-41-4; (4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide) 193275-84-2; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8
CN **(1) Gleevec**; (2) Zarnestra; (3) Hycamtin; **(4) Bch 4556**; (5) Sch 66336; (6) Bms 214662; Psc 833; Ly 335979; G 3139
CO (1) Novartis (United States); (2) Ortho (United States); (3) Glaxo SmithKline (United States); (4) Biochem Pharma (Canada); (5) Schering

Plough (United States); (6) Bristol Myers Squibb (United States)

L89 ANSWER 36 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001169089 EMBASE
TITLE: Latest advances from basic and clinical research in hematology.
AUTHOR: Diaz-Ricart M.
CORPORATE SOURCE: Dr. M. Diaz-Ricart, Hemotherapy Dept. of the Hosp. Clin., IDIBAPS, Villarroel 170, 08036 Barcelona, Spain
SOURCE: Drug News and Perspectives, (2001) 14/1 (50-53). ISSN: 0214-0934 CODEN: DNPEED
COUNTRY: Spain
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB New treatments in hematological malignancies were a focal point of sessions and presentations at the 42nd Annual Meeting of the American Society of Hematology, held December 1-5, 2000, in San Francisco, California, U.S.A. The meeting also provided discussion on pathogen inactivation in blood banking, stem cell transplantation in leukemia as well as nonmalignant diseases, the reparative potential of stem cells, a new oral antithrombotic therapy and a new class of highly selective factor Xa inhibitors. .COPYRGT. 2001 Prous Science.
CT Medical Descriptors:
*leukemia: DT, drug therapy
stem cell transplantation
drug safety
hematologic disease
stem cell
blood bank
antineoplastic activity
conference paper
Drug Descriptors:
anticoagulant agent: PO, oral drug administration
antineoplastic agent: DT, drug therapy
inactine
s 59
glivec
troxatyl
myolotarg
h 376 95
CN (1) Inactine; (2) S 59; **(3) Glivec**; **(4) Troxatyl**; (5) Myolotarg; (6) H 376 95
CO (1) Vitek; (2) Baxter; (3) Novartis; (4) Biochem Corporation; (5) Wyeth; (6) Astra Zeneca

L89 ANSWER 37 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999376440 EMBASE
TITLE: Novel anti-cancer agents in development: Exciting prospects and new challenges.
AUTHOR: Seymour L.
CORPORATE SOURCE: L. Seymour, National Cancer Institute of Canada, Clinical Trials Group, Queens University, 18 Barrie Street, Kingston, Ont. K7L 3N6, Canada
SOURCE: Cancer Treatment Reviews, (1999) 25/5 (301-312).

Refs: 105
ISSN: 0305-7372 CODEN: CTREDJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A large number of cancer chemotherapeutic agents are in development, many already undergoing clinical testing. A number of these compounds were designed either to modulate or inhibit molecular targets which have been identified as being critical to the development or control of cancer. Targets for inhibition include matrix metalloproteinases, mediators of signal transduction (**tyrosine kinases**, cyclin dependent kinases and other kinases such as protein kinase C and A) as well as ros expression and prenylation. Classes of potential inhibitory compounds include small molecules, humanized monoclonal antibodies or antisense oligonucleotides. Many of these compounds are relatively well advanced in development. Proof of principle has already been demonstrated in some instances and at least one such compound has been approved for use. Although these new compounds offer exciting opportunities, many bring with them real challenges in terms of the selection of appropriate trial design and surrogate end-points.

CT Medical Descriptors:
drug design
drug targeting
cancer control
signal transduction
oncogene ras
gene expression
prenylation
methodology
cancer: DT, drug therapy
pancreas cancer: DT, drug therapy
lung non small cell cancer: DT, drug therapy
lung small cell cancer: DT, drug therapy
prostate cancer: DT, drug therapy
ovary cancer: DT, drug therapy
musculoskeletal disease: SI, side effect
rash: SI, side effect
anemia: SI, side effect
thrombocytopenia: SI, side effect
gastrointestinal symptom: SI, side effect
liver toxicity: SI, side effect
drug hypersensitivity: SI, side effect
hypotension: SI, side effect
cardiotoxicity: SI, side effect
fatigue: SI, side effect
headache: SI, side effect
fever: SI, side effect
human
clinical trial
review
Drug Descriptors:
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: DT, drug therapy
matrix metalloproteinase: EC, endogenous compound

cyclin dependent kinase: EC, endogenous compound
protein tyrosine kinase: EC, endogenous compound
protein kinase c: EC, endogenous compound
cyclic AMP dependent protein kinase: EC, endogenous compound
monoclonal antibody: DV, drug development
antisense oligonucleotide
2' deoxy 3' oxacytidine: CT, clinical trial
2' deoxy 3' oxacytidine: DT, drug therapy
4 [4,4 (chlorophenyl)phenyl] 4 oxo (phenylthiomethyl)butanoic acid: CT, clinical trial
4 [4,4 (chlorophenyl)phenyl] 4 oxo (phenylthiomethyl)butanoic acid: DT, drug therapy
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
aplidine: CT, clinical trial
aplidine: DT, drug therapy
zd 1839: AE, adverse drug reaction
zd 1839: CT, clinical trial
zd 1839: DT, drug therapy
bryostatin: AE, adverse drug reaction
bryostatin: CT, clinical trial
bryostatin: DT, drug therapy
isis 3521: AE, adverse drug reaction
isis 3521: CT, clinical trial
isis 3521: DT, drug therapy
cgp 69846a: CT, clinical trial
cgp 69846a: DT, drug therapy
flavopiridol: CT, clinical trial
flavopiridol: DT, drug therapy
sch 66366: CT, clinical trial
sch 66366: DT, drug therapy
batimastat: CT, clinical trial
batimastat: DT, drug therapy
marimastat: AE, adverse drug reaction
marimastat: CT, clinical trial
marimastat: DT, drug therapy
ag 3340: AE, adverse drug reaction
ag 3340: CT, clinical trial
ag 3340: DT, drug therapy
cgs 27023a: AE, adverse drug reaction
cgs 27023a: CT, clinical trial
cgs 27023a: DT, drug therapy
bms 275291: CT, clinical trial
bms 275291: DT, drug therapy
col 3: CT, clinical trial
col 3: DT, drug therapy
a 177430: CT, clinical trial
a 177430: DT, drug therapy
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: CT, clinical trial
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: DT, drug therapy
unindexed drug
[6,7 bis(2 methoxy ethoxy)quinazoline 4 yl](3 ethynylphenyl)amine: AE, adverse drug reaction
[6,7 bis(2 methoxy ethoxy)quinazoline 4 yl](3 ethynylphenyl)amine: CT, clinical trial
[6,7 bis(2 methoxy ethoxy)quinazoline 4 yl](3 ethynylphenyl)amine: DT,

drug therapy
cgp 59326: CT, clinical trial
cgp 59326: DT, drug therapy
epidermal growth factor receptor antibody
RN (cyclin dependent kinase) 150428-23-2; (protein **tyrosine kinase**) 80449-02-1; (protein kinase c) 141436-78-4; (doxorubicin) 23214-92-8, 25316-40-9; (fluorouracil) 51-21-8; (isis 3521) 151879-73-1; (cgp 69846a) 177075-18-2; (flavopiridol) 146426-40-6; (batimastat) 130370-60-4, 130464-84-5; (marimastat) 154039-60-8; (ag 3340) 195008-93-6; (cgs 27023a) 169799-04-6
CN (1) Bb 94; (2) Bb 2516; (3) Ag 3340; (4) Cgs 27023a; (5) Cgp 59326; (6) Bay 12 9566; (7) Bms 275291; (8) Col 3; (9) A 177430; (10) Zd 1839; (11) Pd 153035; (12) Cp 358774; (13) C 225; (14) Isis 3521; (15) Isis 5132; (16) Sch 66366; **Bch 4556**
CO (2) British Biotechnology; (3) Agouron; (5) Novartis; (6) Bayer; (7) Bristol Myers Squibb; (8) Collagenex; (9) Abbott; (10) Astra; (11) Parke Davis; (12) Pfizer; (13) Imclone; (15) Isis; (16) Schering Plough; Abgenix; Genentech; Sugen; Hybridon; Kyowa Hakko Kogyo; Hoechst Marion Roussel; Medarex; Merck; Janssen

L89 ANSWER 38 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:152475 BIOSIS
DOCUMENT NUMBER: PREV200200152475
TITLE: Phase II study of TroxatylTM in patients with chronic myeloid leukemia in blastic phase (CML-BP).
AUTHOR(S): Giles, Francis [Reprint author]; Feldman, Eric; Cortes, Jorge [Reprint author]; Faderl, Stefan [Reprint author]; Larson, Richard; Mamus, Steven; Thomas, Deborah [Reprint author]; Garcia-Manero, Guillermo [Reprint author]; O'Brien, Susan [Reprint author]; Beran, Milsolav [Reprint author]; Talpaz, Moshe [Reprint author]; Kantarjian, Hagop [Reprint author]
CORPORATE SOURCE: UT MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 258b. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002
ED Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002
AB **Troxatyl** triphosphate (converted by the intracellular phosphorylation of **Troxatyl**) is a potent inhibitor and chain terminator for human cellular DNA polymerases and was a unique pattern of cellular uptake and metabolism. On a Phase I study, **Troxatyl** had significant antileukemia activity in patients with refractory disease. (Giles et al, JCO: 19:762:2001). The recommended single agent dose was defined as 8 mg/m2/day daily for 5 days. On a subsequent Phase II study, 6 patients with CML-BP of 16 evaluable (37%) achieved a return to chronic phase disease. (Giles et al, JCO: In press). Three of the 6 responding patients received **Troxatyl** as first therapy for CML-BP; one patient had failed STI571 as prior sole therapy for CML-BP. A multicenter Phase II study of **Troxatyl** 8 mg/m2/day daily for 5 days for patients with CML-BP who have received no prior chemotherapy for CML-BP is

being conducted. Patients who have received **Gleevec** therapy as sole prior therapy for CML-BP are also eligible. Twenty-six patients, 17 male, 26 performance score ltoreq2, median age 54 years (range 31-84) have been entered on study to date, 13 (50%) patients received **Troxatyl** as first therapy for CML-BP, 13 (50%) had failed prior **Gleevec** therapy for CML-BP. Response definitions are as follows: Complete hematologic response (CHR) requires normalization of peripheral counts and differentials with ltoreq5% marrow blasts for at least 4 weeks. Hematologic improvement (HI) is as with CHR but with persistence of thrombocytopenia less than 100X109/L and few immature peripheral cells. A partial hematologic response (PHR) is as per CHR, but allows persistence of, though gtoreq50% reduction of, palpable splenomegaly and thrombocytosis (platelets>450X109/L), or the presence of few immature peripheral cells. Back to second chronic phase (BCP) requires disappearance of BP features and return to chronic phase CML features, i.e., peripheral blasts <15%, peripheral blasts+promyelocytes <30%, peripheral basophils <20%, and platelets >100X109/L. In patients with extramedullary disease (EMD), complete response (CR) requires CHR plus disappearance of all EMD. PR in patients with EMD require at least a 50% reduction in all EMD. Twenty-one patients who have received a total of 40 cycles (range 1 to 4) of **Troxatyl** therapy are currently evaluable for response - 1 PR, 1 HI, 1 BCP, and 1 CR in a patient with EMD have been recorded to date. Four patients died during cycle 1 of therapy - one with a CVA, 3 with sepsis/progressive disease. Extramedullary grade 3 or 4 attributable adverse events in the first cycle of therapy included skin rash (3), hyperbilirubinemia (3), hand foot syndrome (1), colitis (1). One patient developed Sweets Syndrome during 1st cycle of therapy - this subsequently completely resolved. Median survival in the study cohort is 9 months with 33% of patients alive at 1 year. **Troxatyl** has significant activity in patients with CML-BP. Accrual continues on this study.

CC General biology - Symposia, transactions and proceedings . 00520
Cytology - Animal 02506
Cytology - Human 02508
Pathology - Therapy 12512
Metabolism - Metabolic disorders 13020
Digestive system - Pathology 14006
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Integumentary system - Pathology 18506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Toxicology - General and methods 22501
Toxicology - Pharmacology 22504
Neoplasms - Immunology 24003
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Neoplasms - Blood and reticuloendothelial neoplasms 24010
Gerontology - 24500
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - General and methods 36001

IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Hematology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pharmacology

IT Parts, Structures, & Systems of Organisms
basophil: blood and lymphatics, immune system; marrow blast: blood and lymphatics; platelet: blood and lymphatics; spleen: blood and

lymphatics, immune system
IT Diseases
chronic myeloid leukemia in blastic phase: blood and lymphatic disease, neoplastic disease, drug therapy
IT Diseases
colitis: digestive system disease, toxicity
Colitis (MeSH)
IT Diseases
extramedullary disease: disease-miscellaneous
IT Diseases
hand foot syndrome: toxicity
IT Diseases
hyperbilirubinemia: metabolic disease, toxicity
Hyperbilirubinemia (MeSH)
IT Diseases
sepsis: infectious disease
Sepsis (MeSH)
IT Diseases
splenomegaly: blood and lymphatic disease
Splenomegaly (MeSH)
IT Diseases
sweet syndrome: integumentary system disease, toxicity
IT Diseases
thrombocytopenia: blood and lymphatic disease, drug-induced
Thrombocytopenia (MeSH)
IT Diseases
thrombocytosis: blood and lymphatic disease, drug-induced
Thrombocytosis (MeSH)
IT Chemicals & Biochemicals
Troxatyl: antineoplastic-drug, Phase II clinical trial
IT Miscellaneous Descriptors
complete hematologic response; partial hematologic response; Meeting Abstract
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: adult, aged, aged/80 and over, female, male, middle age, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L89 ANSWER 39 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-34978 DRUGU T
TITLE: Novel therapies for myeloplastic syndromes.
AUTHOR: Faderl S; Kantarjian H M
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Cancer (101, No. 2, 226-41, 2004) 4 Fig. 6 Tab. 132 Ref.
CODEN: CANCAR ISSN: 0008-543X
AVAIL. OF DOC.: Department of Leukemia, Box 428, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, U.S.A. (e-mail: sfaderl@mdanderson.org).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Novel treatments for myelodysplastic syndromes (MDS) are reviewed. Clinical features, diagnosis, classification, prognostic factors and biology of MDS are briefly discussed. Treatment is reviewed with

reference to supportive care, hematopoietic growth factors, immunomodulation, farnesyl transferase inhibitors (FTI), **imatinib**, angiogenesis inhibitors, anti-tumor necrosis factor-alpha (anti-TNF-alpha) therapies, arsenicals, epigenetic therapy, high-intensity therapy, chemotherapy and stem cell transplantation. Efficacy, results of clinical trials, doses and toxicity are discussed.

L89 ANSWER 40 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-42053 DRUGU T P
TITLE: New nucleoside analogs in the treatment of hematological disorders.
AUTHOR: Szafraniec S I; Stachnik K J; Skierski J S
CORPORATE SOURCE: Nat.Inst.Public-Health-Warsaw
LOCATION: Warsaw, Pol.
SOURCE: Acta Pol.Pharm. (61, No. 3, 223-32, 2004) 84 Ref.
CODEN: APPHAX ISSN: 0001-6837
AVAIL. OF DOC.: Flow Cytometry Laboratory, National Institute of Public Health, 30/34 Chelmska Str, 00-725 Warsaw, Poland. (J.S.S.). (e-mail: skierski@il.waw.pl).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The new nucleoside analogs (tezacitabine, **troxacitabine**, clofarabine, nelarabine, decitabine, 2'-C-cyano-2'-d-1-beta-D-arabino pentofuranosylcytosine (CNDAC) and 3'ethynylocytidine (ECyD) in the treatment of hematological disorders are reviewed. The mechanism of action, preclinical trials and clinical trials of tezacitabine, **troxacitabine**, clofarabine, nelarabine, decitabine and CNDAC are described.

L89 ANSWER 41 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-21310 DRUGU T P S
TITLE: **Troxacitabine.**
AUTHOR: Gourdeau H; Jolivet J
CORPORATE SOURCE: ShireBioChem
LOCATION: Quebec, Que., Can.
SOURCE: Bull.Cancer (91, No. 3, 213-18, 2004) 2 Fig. 1 Tab. 43 Ref.
CODEN: BUCABS ISSN: 0007-4551
AVAIL. OF DOC.: ShireBioChem Inc., 275, boulevard Armand-Frappier, Quebec, Canada, H7V 4A7. (E-mail: henriettegourdeau@videotron.com).
LANGUAGE: French
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The antitumor activity of deoxycytidine analog **troxacitabine** (TX) in preclinical studies and phase I and II clinical trials is reviewed.Unlike lamivudine, gemacitabine and cytarabine (AC), TX has a non-natural beta-L stereochemical configuration. TX has a large spectrum of activity against in-vitro and animal cancer models, including vinblastine and doxorubicin resistant tumors but toxicity is greater in primates than rodents. TX has promising clinical activity against refractory solid tumors and acute leukemias (with AC, idarubicin and topotecan), dose-limiting side-effects are mainly hematological and cutaneous (eruption, stomatitis and hand-foot syndrome). Further studies are required.

L89 ANSWER 42 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-29719 DRUGU T
TITLE: Emerging treatments in acute myeloid leukaemia.

AUTHOR: Kell J
CORPORATE SOURCE: Univ.Wales
LOCATION: Cardiff, U.K.
SOURCE: ; Expert Opinion Emerg.Drugs (9, No. 1, 55-71, 2004) 4 Fig. 3 Tab. 211 Ref.
CODEN: ; 4023
AVAIL. OF DOC.: University Hospital of Wales, Cardiff, CF14 4XW, Wales. (e-mail: jonathan.kell@cardiffandvale.wales.nhs.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The scientific rationale of emerging treatments (**imatinib**, manumycin, alpha-hydroxyfarnesyl phosphonic acid, tipifarnib, SCH-66336, BMS-214662, anti-CD33 mAb, gemtuzumab ozogamicin, SU-5416, CEP-701, CT-53518, PKC-412, AG-1296, AG-1295, gemcitabine, clofarabine, **troxacitabine**, 5-azacytidine, decitabine, zebularine, depsipeptide, valproate) in acute myeloid leukemia (AML) is reviewed. The current treatments (daunorubicin, Ara-C, etoposide, idarubicin, mitoxantrone) for AML are discussed. The generally favorable side effect profiles of these drugs and the good oral bioavailability of at least some of the agents make them particularly attractive treatment options in the older population or patients not considered fit enough for intensive chemotherapy.

L89 ANSWER 43 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-10803 DRUGU P
TITLE: **Troxatyl** and STI571 combination therapy for chronic myeloid leukemia: preclinical in vitro and in vivo evaluation.
AUTHOR: Orsolic N; Giles F; Beran M; Cortes J; Albitar M; Kantarjian H; Verstovsek S
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Blood (100, No. 11, Pt. 1, 786a, 2002) 2 Ref.
CODEN: BLOOAW ISSN: 0006-4971
AVAIL. OF DOC.: Leukemia, The University of Texas, MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The effects of **Troxatyl** (TX, **troxacitabine**) and **imatinib** (IM, **STI-571**) were investigated in-vitro in chronic myeloid leukemia (CML) KBM5 and KBM7 cells, IM-resistant sublines KBM5-R and KBM7-R, cells from patients with CML and in-vivo after i.p. administration in mice bearing KBM5 or KBM5-R cells. TX and IM showed a synergistic cytostatic activity both in in-vitro and in-vivo studies. In conclusion, the results show that TX has activity in late stage CML and that combining it with IM is a very reasonable clinical approach. (conference abstract: 44th Annual Meeting of the American Society of Hematology, Philadelphia, Pennsylvania, USA, 2002).

L89 ANSWER 44 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-17334 DRUGU T S
TITLE: Phase II study of **Troxatyl** in patients with chronic myeloid leukemia in blastic phase (CML-BP).
AUTHOR: Giles F; Feldman E; Cortes J; Faderl S; Larson R; Mamus S; Thomas D; Garcia Manero G; O'Brien S; Beran M; Talpaz M; Kantarjian H

CORPORATE SOURCE: Anderson-Cancer-Cent.; Univ.Chicago; Univ.Cornell
LOCATION: Houston, Tex., New York, N.Y., Chicago, Ill.; Orlando, Fla., USA
SOURCE: Blood (98, No. 11, Pt. 2, 258b, 2001) 1 Ref.
CODEN: BLOOAW ISSN: 0006-4971
AVAIL. OF DOC.: UT MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The efficacy of **troxacitabine** (**Troxatyl**) was investigated in 26 patients with chronic myeloid leukemia in blastic phase (CML-BP) in a phase II study. Side-effects included skin rash, hyperbilirubinemia, hand foot syndrome, colitis, and Sweets syndrome. The result showed that **Troxatyl** had significant activity in these CML-BP patients. (conference abstract: 43rd Annual Meeting of the American Society of Hematology, Orlando, Florida, USA, 2001).

L89 ANSWER 45 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-12589 DRUGU T S
TITLE: **Troxatyl** is effective in non-lymphoid blastic phase chronic myeloid leukemia (CML-BP).
AUTHOR: Giles F; Talpaz M; Bivins C; Jolivet J; Kantarjian H
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Eur.J.Cancer (37, Suppl. 6, S35, 2001) 2 Ref.
CODEN: EJCAEL ISSN: 0964-1947
AVAIL. OF DOC.: University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The use of **troxacitabine** (**Troxatyl**) to treat 17 patients with non-lymphoid blastic phase chronic myeloid leukemia (CML-BP) is reported. Side-effects included rash, hand-foot syndrome and mucositis. Median survival was over 52 wk. **Troxatyl** as a single agent in CML-BP is under study in Phase II trial. (conference abstract: 11th European Cancer Conference, Lisbon, Portugal, 2001).

=> d iall abeq tech abex 46-
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L89 ANSWER 46 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-048472 [05] WPIX
DOC. NO. CPI: C2005-016552
TITLE: Prevention/treatment/reduction of the occurrence of vascular stenosis or restenosis following angioplasty comprises administration of a platelet derived growth factor receptor inhibitor and a phosphoinositide-3 kinase pathway inhibitor.
DERWENT CLASS: B04 B05
INVENTOR(S): SUKHATME, V P
PATENT ASSIGNEE(S): (BETH-N) BETH ISRAEL DEACONESS MEDICAL CENT
COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004108130	A1	20041216	(200505)*	EN	48	A61K031-40

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004108130	A1	WO 2004-US17273	20040601

PRIORITY APPLN. INFO: US 2003-475295P 20030603
INT. PATENT CLASSIF.:
MAIN: A61K031-40
SECONDARY: A61K031-44; A61K031-519; A61K031-551
BASIC ABSTRACT:
WO2004108130 A UPAB: 20050124
NOVELTY - Prevention or treatment or reduction of the occurrence of vascular stenosis or restenosis following angioplasty comprises administration of a first compound (1) capable of inhibiting platelet derived growth factor receptor (PDGFR) and a phosphoinositide-3 kinase (PI3K) pathway inhibitor (2).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a pharmaceutical composition (A) comprising (1) and (2); and
(2) a kit comprising (1), (2), (3) and instructions for administration of (1), (2) and (3) to a patient diagnosed with or at risk of developing stenosis or restenosis following angioplasty.

ACTIVITY - Vasotropic.

MECHANISM OF ACTION - Platelet derived growth factor receptor beta (PDGFR- beta) inhibitor; Phosphoinositide-3 kinase (PI3K) pathway inhibitor.

USE - (1) along with (2) is useful in the prevention/treatment/reduction of the occurrence of vascular stenosis or restenosis (characterized by the migration of smooth muscle cells into the intima; the proliferation of vascular smooth muscle cells; or the deposition of extracellular matrix) following angioplasty and the use of a stent for treatment. (1) with (2) is also useful to reduce or prevent vascular smooth muscle cell hyperplasia (all claimed). The ability of (1) (**imatinib** mesylate) and (2) (rapamycin) to prevent migration of smooth muscle cells was tested using human aortic vascular smooth muscle cells. The results showed that the percentage inhibition was 70-80%.

ADVANTAGE - (1) and (2) acts synergistically.

Dwg.0/1
FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B01-A02; B01-B01; B01-B02; B02-C01; B02-R; B02-T; B03-H; B04-A03; B04-A06; B04-A08C2; B04-A10B; B04-C01B; B04-C01H; B04-G04; B04-G21; B04-H05A; B04-H19; B04-N02; B04-N06; B05-B01E; B05-B01J; B05-B01P; B06-A01; B06-A02; B06-D01; B06-D02; B06-D03; B06-D04; B06-D06; B06-D07; B06-D09;

B06-D17; B06-D18; B06-E05; B06-F03; B07-A01; B07-A02; B07-A03; B07-D03; B07-D04C; B07-D04D; B07-D05; B07-D08; B07-D12; B10-A09B; B10-B02D; B10-B02E; B10-B03B; B10-C03; B10-C04A; B10-C04D; B10-C04E; B10-E02; B14-D05C; B14-D06C; B14-D07A1; B14-F01G; B14-F02F2; B14-F04; B14-G02; **B14-H01B**; B14-J04; B14-J05; B14-L06; **B14-S09**

TECH UPTX: 20050124

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: (1) is an N-phenyl-2-pyrimidine derivative, preferably **imatinib** mesylate. (1) inhibits PDGFR activity stimulated by a PDGF-BB ligand. (2) inhibits the biological activity of any protein on the phosphoinositide-3 kinase (PI3K)/Akt/ mammalian target of rapamycin (mTOR) signaling pathway and also inhibits the biological activity of mTOR. The stent is coated with (1) and (2). (1) and (2) are given in combination with a carrier. The treatment further comprises administration of at least one additional compound (3) such as an angiogenesis inhibitor, an anti-proliferative compound, an immunosuppressive compound, an anti-migratory compound, an anti-platelet agent and an anti-fibrotic compound. The angiogenesis inhibitor is an antibody; an antibody that binds vascular endothelial growth factor-A (VEGF-A); an antibody that binds a VEGF receptor and blocks VEGF binding; avastin; endostatin; angiostatin; restin; tumstatin; TNP-470; 2- methoxyestradiol; thalidomide; a peptide fragment of an antiangiogenic protein; canstatin; arrestin; a VEGF kinase inhibitor; CPTK787; SFH-1; an anti-angiogenic protein; thrombospondin-1; platelet factor-4; interferon-alpha; an agent that blocks TIE-1, TIE-2 or PIH12 signaling; an agent that blocks an extracellular vascular endothelial (VE) cadherin domain; an antibody that binds to an extracellular VE-cadherin domain; tetracycline; penicillamine; vinblastine; cytoxan; edelfosine; tegafur; uracil; curcumin; green tea; genistein; resveratrol; N-acetyl cysteine; captopril; a cyclooxygenase (cox-2) inhibitor; celecoxib or rofecoxib. The anti-proliferative compound is rapamycin; taxol; troglitazone; an agent that inhibits VEGF (preferably an antibody); an agent that inhibits bFGF (preferably an antibody); an antibody that binds bFGF-saporin; a statin; an angiotensin-converting enzyme (ACE) inhibitor; suramin; 17-beta-estradiol; atorvastatin; fluvastatin; lovastatin; pravastatin; simvastatin; cerivastatin; perindopril; quinapril; captopril; captopril; lisinopril; enalapril; fosinopril; cilazapril; ramipril; or a kinase inhibitor. The immunosuppressive compound is prednisone; FTY720; methylprednisolone; a-tocopherol; azathioprine; chlorambucil; cyclophosphamide; an antibody that binds to an interleukin-2 (IL-2) receptor or to cytotoxic T-lymphocyte associated antigen-4 (CTLA-4); methotrexate; mycophenolate mofetil; cyclosporine; an agent that interferes with macrophage function; an agent that inhibits P-selectin PSGL-1; very late antigen-4 (VLA-4); vascular cell adhesion molecule-1 (VCAM-1) or Mac-1 biological function; or FTY720. The anti-migratory compound is cyproheptadine; endothelin receptor antagonist; serotonin receptor antagonist; methysergide; bosentan; YM087; cyproheptadine; ketanserin; or anplag. The anti-platelet agent is aspirin; ticlopidine; cilostazol; dipyridamole; abciximab; clopidogrel; dipyridimole; a glycoprotein iib/iiia inhibitor; an adenosine reuptake inhibitor; an ADP inhibitor; eptifibatide; tirofiban; a phosphodiesterase III inhibitor; or ticlopdipine. The anti-fibrotic compound is blocks tumor growth factor (TGF)-beta signaling or inhibits activation of plasminogen activator inhibitor-1 promoter activity; an antibody that binds to TGF-beta or to a TGF-beta receptor; an antibody that binds to TGF-beta receptor I, II, or III; a kinase inhibitor; an agent that blocks CTGF signaling; an agent that inhibits prolyl hydroxylase; an agent that inhibits procollagen C-proteinase; pirfenidone; silymarin; pentoxifylline; colchicines; embrel;

remicade; an agent that antagonizes TGF-beta; an agent that antagonizes CTGF; and an agent that inhibits VEGF. Preferred Composition: (A) further comprises at least one (3).

ABEX UPTX: 20050124

SPECIFIC COMPOUNDS - The use of **imatinib** mesylate is specifically claimed as (1). The use of rapamycin is specifically claimed as (2).

ADMINISTRATION - Administration of (1) and (2) is oral, parenteral, intravenous, subcutaneous or local. Administration of **imatinib** mesylate is 50-5000 (preferably 100-800) mg/day, orally.

L89 ANSWER 47 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-021162 [02] WPIX
DOC. NO. CPI: C2005-006619
TITLE: Combination useful for treating proliferative disease e.g. breast cancer comprises a chemotherapeutic agent and a histone deacetylase inhibitor.
DERWENT CLASS: B05
INVENTOR(S): ATADJA, P W; REMISZEWSKI, S W; TROGANI, N
PATENT ASSIGNEE(S): (NOVS) NOVARTIS AG; (NOVS) NOVARTIS PHARMA GMBH
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004103358	A2	20041202	(200502)*	EN	43	A61K031-16

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004103358	A2	WO 2004-EP5433	20040519

PRIORITY APPLN. INFO: US 2003-472161P 20030521
INT. PATENT CLASSIF.:
MAIN: A61K031-16
SECONDARY: A61K031-4045; A61K031-4745; A61K031-513; A61K031-704; A61K031-7068; A61K045-06; **A61P035-00**; **A61P035-04**

BASIC ABSTRACT:
WO2004103358 A UPAB: 20050107
NOVELTY - A combination comprises a chemotherapeutic agent (a1) and a histone deacetylase inhibitor (a2) in their free form, salt, or prodrugs, for simultaneous, concurrent, separate or sequential use .

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a commercial package or product comprising (a1) together with instructions for use in combination with (a2), for treating a disease in a mammal, or (a2) together with instructions for use in combination with (a1), for treating a disease in a mammal.

ACTIVITY - Cytostatic; Respiratory-Gen; Nephrotropic; Antiangiogenic; Antipsoriatic; Antiarteriosclerotic; Antiinflammatory; Vasotropic;

Vulnerary.

MECHANISM OF ACTION - Vascular endothelial growth factor family of receptor tyrosine kinases (VEGFR) inhibitor or activator; Tumor growth inhibitor.

The antiproliferative effects of adding N-hydroxy-3-(4-(((2-hydroxyethyl)(2-(1H-indol-3-yl)ethyl)-amino)methyl)phenyl)-2E-2-propenamide (a2') simultaneously, 24 hours after, or 24 hours before adding the chemotherapeutic agent adriamycin to MDA-MB-435P cell line (human breast carcinoma) were examined. The combined effects were assessed using constant ratios of compound concentrations that were 8-fold, 4-fold, 2-fold, 1 -fold, 0 fold, 0 fold and 0 fold of their respective IC50s. To examine whether the combinations were additive, synergistic or antagonistic, isobolograms were plotted and combination indices calculated using the commercial software program CalcuSyn. In isobolograms, the X intercepts indicate the concentrations of one drug which results in a given percentage of growth inhibition and the Y intercepts indicate the concentrations at which the other drug inhibited the growth of the cells. The data point that falls between the axes indicates the concentration of the drug combination that inhibits cell growth. The further above or below this data point deviates from the straight line joining the intercepts, the more antagonistic or synergistic the effect, respectively. Combination data points that fall on or close to the line joining the intercepts indicate additive effects.

Simultaneous incubation of MDA-MB-435P cells with adriamycin and (a2') or treatment with (a2') 24 hours prior to adding adriamycin produced isobologram combination data points close to the line joining the X and Y intercepts. The calculated combination indices were close to 1, indicating additive effects. However, treatment of MDA-MB-435P cells with adriamycin 24 hours prior to (a2') resulted in combination data points far below the line joining the intercepts, indicating strong synergy between the two drugs.

USE - For treatment of proliferative disease e.g. breast cancer, lung cancer, ovarian cancer, lymphoma, head and neck cancer and cancer of the esophagus, stomach, bladder, prostate, uterus and cervix; for treatment or prevention of proliferative diseases including premalignant lesions as well as both solid and undifferentiated malignancies (all claimed); for treatment of leukemias, hyperplasias, fibrosis (e.g. pulmonary or renal fibrosis), angiogenesis, psoriasis, atherosclerosis, and smooth muscle proliferation in blood vessels, such as stenosis or restenosis following angioplasty.

ADVANTAGE - The combination is more efficacious, provides synergistic and additive advantages, both for efficacy and safety; and provides lower safe dosage ranges of each component in the combination.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B02-D; B06-H; B07-H; B08-H; B10-A09B; B10-A15; B10-A18; B14-C03; B14-F01G; B14-F02F2; B14-F07; **B14-H01**; B14-K01; B14-N10; B14-N17B; B14-N17C; **B14-S09**

TECH UPTX: 20050107

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (a1) is DNA topoisomerase I inhibitor; DNA topoisomerase II inhibitor; microtubule active agent; or antimetabolites including agents which are inhibitors of thymidine production, inhibitors of vascular endothethial growth factor, DNA demethylating agents, or protein-tyrosine kinase inhibitors (such as discodermolides and epothilones), or salts or prodrugs of these. (a2) Is a compound of formula (I), preferably a compound of formula (Ia).

R1 = H, halo or 1-6C alkyl (preferably H);

R2 = U1 (preferably H or -CH2-CH2-OH);

U1 = H, 1-10C alkyl, 4-9C (hetero)cycloalkyl, 4-9C heterocycloalkylalkyl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, -(CH2)nC(O)R6, -(CH2)nOC(O)R6, amino acyl, HON-C(O)-CH=C(R1)-aryl-alkyl- or -(CH2)nR7;
R3, R4 = H, 1-6C alkyl, acyl or acylamino (preferably H); or
R3+R4 = C=O, C=S or C=NR8; or
NR2R3 = 4-9C heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or a mixed aryl or non-aryl polyheterocycle ring;
R5 = H, T1, acyl, aromatic polycycle, non-aromatic polycycle, mixed aryl and non-aryl polycyle, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle;
T1 = 1-6C alkyl, 4-9C (hetero)cycloalkyl, (hetero)aryl or (hetero)arylalkyl;
X,Y = H, halo, 1-4C alkyl, NO2, C(O)R1, OR9, SR9, CN or NR10R11 (preferably H);
R6 = H, T1, cycloalkylalkyl, OR12 or NR13R14;
R7 = OR15, SR15, S(O)R16, SO2R17, NR13R14 or NR12SO2R6;
R8 = T1, H, OR15 or NR13R14;
R9 = 1-4C alkyl or C(O)-alkyl;
R10,R11 = H or R9;
R12 = T1, H, 4-9C heterocycloalkylalkyl or mixed aryl and non-aryl polycyle;
R13, R14 = T1, H or amino acyl;
R13R14N = 4-9C heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle;
R15 = T1, H or (CH2)mZR12;
R16 = T1, polyheteroaryl or (CH2)mZR12;
R17 = T1, aromatic polycycle, polyheteroaryl or NR13R14;
n, n1, n3, m = 0 - 6;
n2, n3 = 0 - 6 (preferably 0 or 1);
Z = O, NR13, S or S(O);
R18 = H, halo, 12-6C alkyl, 3-7C cycloalkyl or (hetero)aryl (preferably H, fluoro, chloro, bromo, 1-4C alkyl, 3-7C cycloalkyl, phenyl or heteroaryl);
R20 = H, 1-6C alkyl, 3-9C cycloalkyl-1-6C alkyl, (hetero)aryl, (hetero)arylalkyl, acyl or sulfonyl;
A1 = 1 - 3 substituents selected from H, 1-6C alkyl, -OR19, halo, alkylamino, aminoalkyl, halo or heteroarylalkyl;
R19 = H, T1 or -(CH2CH=CH(CH3)(CH2))1-3H;
p = 0 - 3;
q, r = 0 - 5 (preferably 1 - 3);
R'2 = U1 (preferably H or -(CH2)sCH2OH);
s = 1 - 3.
Provided that:
(1) when n1 is 1-6, each carbon atom can be optionally substituted with R3 and/or R4;
(2) when one of n2 and n3 is 0, then the other of n2 and n3 is 1;
(3) when q is 1 - 5, then r is 0; and
(4) when q is 0, then r is 1 - 5.

ABEX UPTX: 20050107

SPECIFIC COMPOUNDS - (a1) Is adriamycin, epothilone B or D, 5-fluorouracil, camptothecin, gimatecan, **imatinib** (**Gleevec**), PTK787 (RTM; 1-(4-chloroanilino)-4-(pyridylmethyl)-phthalazine succinate), 5-Aza dC (decitabine) or 5-azacytidine. (a2) is N-hydroxy-3-(4-(((2-hydroxyethyl)(2-(1H-indol-3-yl)ethyl)-amino)methyl)phenyl)-2E-2-propenamide (a2'), N-hydroxy-3-(4-(((2-(1H-indol-3-yl)ethyl)amino)methyl)phenyl)-2E-2- propenamide or N-hydroxy-3-(4-(((2-(2-methyl-1H-indol-3-yl)ethyl)-amino)methyl)phenyl)-2E-2-propenamide

ADMINISTRATION - Administration is preferably oral in the form of a tablet, capsule or syrup, or as parenteral injections. E.g. adriamycin, 5-fluorouraccil and camptothecin are each administered at 100-1500

(preferably 200-1000) mg/day in one or two doses.

L89 ANSWER 48 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-580619 [56] WPIX
CROSS REFERENCE: 2004-561737 [54]; 2004-580620 [56]; 2004-580621 [56]
DOC. NO. CPI: C2004-211614
TITLE: Use of lonidamine in combination with one or more additional chemotherapeutic agents (e.g. 2-deoxy-D-glucose) for the treatment of cancers like non-small-cell lung cancer, breast cancer, prostate cancer and colorectal cancer.
DERWENT CLASS: B05
INVENTOR(S): TIDMARSH, G
PATENT ASSIGNEE(S): (THRE-N) THRESHOLD PHARM INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004064734	A2	20040805	(200456)*	EN	62	A61K000-00

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004064734	A2	WO 2004-US1138	20040116

PRIORITY APPLN. INFO: US 2003-458663P 20030328; US 2003-441110P 20030117; US 2003-442344P 20030123
INT. PATENT CLASSIF.:
MAIN: A61K000-00
BASIC ABSTRACT:
WO2004064734 A UPAB: 20040901
NOVELTY - Treatment of cancer comprises administration of lonidamine (I) in combination with one or more additional chemotherapeutic agents (II) to mammals.

ACTIVITY - Cytostatic; Antithyroid; Dermatological; Fungicide; Anti-HIV; Osteopathic; Cardiovascular-Gen.; CNS-Gen.; Gastrointestinal-Gen.

MECHANISM OF ACTION - HIF-1 alpha inhibitor; VegF inhibitor.

USE - Lonidamine (I) in combination with one or more of (II) is useful for the treatment of cancer (breast cancer, skin cancer, bone cancer, prostate cancer, liver cancer, lung cancer, brain cancer, cancer of the larynx, gall bladder, pancreas, rectum, parathyroid, thyroid, adrenal, neural tissue, head and neck, colon, stomach, bronchi, kidneys, basal cell carcinoma, squamous cell carcinoma of both ulcerating and papillary type, metastatic skin carcinoma, osteo sarcoma, Ewing's sarcoma, veticulum cell sarcoma, myeloma, giant cell tumor, small-cell lung tumor, islet cell tumor, primary brain tumor, acute and chronic lymphocytic and granulocytic tumors, hairy-cell tumor, adenoma, hyperplasia, medullary carcinoma, pheochromocytoma, mucosal neuronomas, intestinal

gangIloneuromas, hyperplastic corneal nerve tumor, marfanoid habitus tumor, Wilm's tumor, seminoma, ovarian tumor, leiomyomater tumor, cervical dysplasia and in situ carcinoma, neuroblastoma, retinoblastoma, soft tissue sarcoma, malignant carcinoid, topical skin lesion, mycosis fungoide, rhabdomyosarcoma, Kaposi's sarcoma, osteogenic and other sarcoma, malignant hypercalcemia, renal cell tumor, polycythermia vera, adenocarcinoma, glioblastoma multiforma, leukemias, lymphomas, malignant melanomas or epidermoid carcinomas) (claimed).

The effect of (I) in treating cancers was tested using biological assays. The results showed lonidamine as a highly useful agent in combination therapies for all solid tumors.

ADVANTAGE - Cancer is treated by administering lonidamine or a lonidamine analog at a lower dose that may be continued to be administered for weeks to months while limiting or eliminating the unwanted, albeit usually mild, side effects reported for higher doses of lonidamine (principally myalgia and testicular pain).

Dwg.0/4

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B01-A02; B01-B01; B01-D02; B02-B; B02-C01; B02-D; B02-N; B02-O; B02-P; B02-R; B02-S; B02-T; B04-C01B; B04-G21; B04-L05; B05-A03B; B06-A01; B06-A02; B06-A03; B06-D04; B06-D05; B06-D06; B06-D08; B06-D09; B06-D11; B06-D16; B06-D18; B06-E05; B06-F03; B07-A02; B07-A04; B07-D01; B07-D04C; B07-D09; B07-D12; B07-D13; B07-E02; B07-F01; B08-D02; B08-D03; B10-A07; B10-A13D; B10-A16; B10-B01A; B10-B02A; B10-B02E; B10-B02J; B10-B03B; B10-B04; **B14-H01**; B14-L06; **B14-S09**

TECH UPTX: 20040901

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: Chemotherapeutic agent (II) is selected from busulfan, improsulfan, piposulfan, benzodepa, carboquone, 2-deoxy-D-glucose, meturedepa, uredepa, altretamine, **imatinib**, triethylenemelamine, triethylenephosphoramide, triethylenethiophosphoramide, trimethylolomelamine, chlorambucil, chlornaphazine, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard, carmustine, chlorozotocin, fotemustine, nimustine, ranimustine, dacarbazine, mannomustine, mitobronitol, mitolactol, pipobroman, aclacinomycins, actinomycin F(1), anthramycin, azaserine, bleomycin, cactinomycin, carubicin, carzinophilin, chromomycin, dactinomycin, daunorubicin, daunomycin, 6-diazo-5-oxo-1-norleucine, mycophenolic acid, nogalamycin, olivomycin, peplomycin, plicamycin, porfiromycin, puromycin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin, denopterin, pteropterin, trimetrexate, fludarabine, 6-mercaptopurine, thiamiprine, thioguanine, ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, 5-fluorouracil, tegafur, L-asparaginase, pulmozyme, aceglatone, aldophosphamide glycoside, aminolevulinic acid, amsacrine, bestrabucil, bisantrene, carboplatin, defofamide, demecolcine, diaziquone, elfomithine, elliptinium acetate, etoglucid, flutamide, gallium nitrate, hydroxyurea, interferon-alpha, interferon-beta, interferon-gamma, interleukin-2, lentinan, mitoguazone, mitoxantrone, mopidamol, nitracrine, pentostatin, phenamet, pirarubicin, podophyllinic acid, 2-ethylhydrazide, procarbazine, razoxane, sizofiran, spirogermanium, paclitaxel, tamoxifen, teniposide, tenuazonic acid, triaziquone, 2,2',2-trichlorotriethylamine, urethan, vinblastine or vincristine) (preferably gemcitabine, a taxane or 2-deoxy-D-glucose). (II) is both 2-deoxy-2-glucose and one or more agents of cisplatin, carboplatin, taxol, taxotere, cytoxan, vincristine,

adriamycin, captosar, 5-fluorouracil, levamisole, prednisone, mitoxantrone, herceptin or vinorelbine (preferred).
Preferred Method: For the treatment of non-small-cell lung cancer, (I) is co-administered with either cisplatin or carboplatin together with an anti-cancer agent (taxol, taxotere, gemcitabine or vinorelbine).
For the treatment of breast cancer, (I) is co-administered with either taxol or taxotere and herceptin; or cytoxan and 5-fluorouracil and either adriamycin or methotrexate.
For the treatment of prostate cancer, (I) is co-administered with either prednisone or taxotere, and optionally with mitoxantrone (if prednisone is administered).
For the treatment of colorectal cancer, (I) is co-administered with either captosar or 5-fluorouracil and levamisole.
For the treatment of ovarian cancer, either (I) is co-administered with cisplatin or carboplatin, together with either taxol or taxotere; or (I) is co-administered with cisplatin or carboplatin; or cytoxan, vincristine, and prednisone, and optionally together with adriamycin.
For the treatment of cancers (particularly head or neck cancer), lonidamine or its analog in combination is administered with hyperfractionated radiation therapy. (I) can also be administered with a HIF-1 alpha inhibitor or a VegF inhibitor (particularly avastin to treat colon cancer, pancreatic cancer or renal cell carcinoma).

ABEX UPTX: 20040901

ADMINISTRATION - Administration of (I) is greater than 300 and less than 500 mg/day (low dosage), orally, parenterally, transdermally, rectally or by inhalation spray or intraprostetic injection.

L89 ANSWER 49 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-460982 [43] WPIX
DOC. NO. CPI: C2004-172134
TITLE: Use of cell cycle checkpoint activator and oncogenic kinase modulator for treatment of cancer e.g. lung cancer, malignant melanoma and childhood leukemia.
DERWENT CLASS: B02
INVENTOR(S): LI, C; LI, Y
PATENT ASSIGNEE(S): (ARQU-N) ARQULE INC
COUNTRY COUNT: 107
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004050033	A2	20040617	(200443)*	EN	40	A61K000-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
AU 2003293333	A1	20040623	(200472)			A61K000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004050033	A2	WO 2003-US38405	20031202
AU 2003293333	A1	AU 2003-293333	20031202

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003293333	A1 Based on	WO 2004050033

PRIORITY APPLN. INFO: US 2002-430288P 20021202
INT. PATENT CLASSIF.:
MAIN: A61K000-00
BASIC ABSTRACT:
WO2004050033 A UPAB: 20040709
NOVELTY - Treatment of cancer comprises administration of a cell cycle checkpoint activator (A) or its derivative or analog, and an oncogenic kinase modulator (B).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for the treatment of a malignancy comprising separate vials containing beta -lapachone and (B), with instructions for administering beta -lapachone first.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Cell cycle checkpoint activator; Oncogenic kinase modulator.

USE - (A) and (B) are useful in the treatment of lung cancer, breast cancer, colon cancer, ovarian cancer, prostate cancer, malignant melanoma, non-melanoma skin cancers, hematologic tumors, hematologic tumors, hematologic malignancies, childhood leukemia, childhood lymphomas, multiple myeloma, Hodgkin's disease, lymphomas of lymphocytic origin, lymphomas of cutaneous origin, acute leukemia, chronic leukemia, acute lymphoblastic leukemia, acute myelocytic leukemia, chronic myelocytic leukemia, plasma cell neoplasm, lymphoid neoplasm, cancers associated with AIDS or preferably multiple myeloma, chronic myelogenous leukemia, pancreatic cancer or non-small cell lung cancer in human (claimed).

The ability of (B) (2 micro M) along with (A) (20 micro M) to treat cancer was assessed in K562 cells (a human chronic myelogenous leukemia (CML) cell line). Results showed that the percentage viability of cells was found to be 3.8%.

ADVANTAGE - (A) and (B) are synergistic.

Dwg.0/2
FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B06-A02; B07-D04C; B07-D11; B07-D12; B14-D06; **B14-H01**; B14-L01; **B14-S09**
TECH UPTX: 20040709
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (B) is a tyrosine kinase modulator, which is an epidermal growth factor receptor signal transduction pathway modulator or preferably a breakpoint cluster region (Bcr)-Abl signal transduction pathway modulator. (A) further comprises a pharmaceutically acceptable water solubilizing carrier molecule such as poloxamer, povidone K17, povidone K12, tween 80, ethanol, cremophor/ethanol, polyethylene glycol 400, propylene glycol, trappsol, or alpha-, beta- or delta-cyclodextrin. (A) is contained in a first vial and (B) is contained in a second vial.

Preferred Method: (B) is administered simultaneously with, sequentially, preceding or preferably following (within 24 hours) administration of (A).
ABEX UPTX: 20040709
SPECIFIC COMPOUNDS - The use of beta-lapachone is specifically claimed as (A). The use of **imatinib** is specifically claimed as (B).

ADMINISTRATION - Dosage of (A) is 100 - 500000 (preferably 10000 - 150000) ug/kg/day, and of (B) is 10 - 2000 (preferably 250) mg/day, and administration is intravenous, intraperitoneal or preferably oral.

L89 ANSWER 50 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-440878 [41] WPIX
DOC. NO. CPI: C2004-165247
TITLE: Use of indolinone compounds which are receptor tyrosine kinase inhibitors, in combination with at least one chemotherapeutic agent for treatment of cancer, e.g. colon cancer and non-small cell lung cancer.
DERWENT CLASS: B02
INVENTOR(S): ABRAMS, T; CHERRINGTON, J; MURRAY, L; PRYER, N; CHERRINGTON, J M
PATENT ASSIGNEE(S): (SUGE-N) SUGEN INC
COUNTRY COUNT: 107
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004045523	A2	20040603	(200441)*	EN	87	A61K000-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
US 2004152759	A1	20040805	(200452)			A61K031-4439
AU 2003290943	A1	20040615	(200470)			A61K000-00
NL 1024779	C2	20041109	(200505)			A61K031-404

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004045523	A2	WO 2003-US36526	20031114
US 2004152759	A1 Provisional	US 2002-426386P	20021115
		US 2003-712296	20031114
AU 2003290943	A1	AU 2003-290943	20031114
NL 1024779	C2	NL 2003-1024779	20031114

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003290943	A1 Based on	WO 2004045523

PRIORITY APPLN. INFO: US 2002-426386P 20021115; US 2003-712296 20031114
INT. PATENT CLASSIF.:
MAIN: A61K000-00; A61K031-404; A61K031-4439
SECONDARY: A61K031-405; A61K031-4745; A61K031-513; A61K031-704; A61K033-24; **A61P035-00**

BASIC ABSTRACT:
WO2004045523 A UPAB: 20040629
NOVELTY - Treatment of cancer comprises administration of indolinone compounds (I) or their salts, hydrates or solvates in combination with at least one chemotherapeutic agent (A) (e.g. microtubule interference agents, topoisomerase inhibitors, alkylating agents and/or kinase inhibitors).

DETAILED DESCRIPTION - Treatment of cancer comprises administration of indolinone compounds of formula (I) or their salts, hydrates or solvates in combination with at least one chemotherapeutic agent (A) (e.g. microtubule interference agents, topoisomerase inhibitors, alkylating

agents, thymidylate synthase inhibitors, irreversible steroidal aromatase inactivators, anti-metabolites, pyrimidine antagonists, purine antagonists, ribonucleotide reductase inhibitors and/or kinase inhibitors).

R = H, OH, (cyclo)alkyl, (hetero)aryl, alkoxy, heterocyclic or NH2;

R1 = halo, (halo)alkyl, (halo)alkoxy, cycloalkyl, heterocyclic, OH, C(O)-R8, NR9R10, NR9C(O)-R12 or C(O)NR9R10;

R2 = alkyl, (hetero)aryl, C(O)-R8 or SO2R';

R' = alkyl, (hetero)aryl, NR9R10 or alkoxy;

R5 = H, (halo)alkyl, cycloalkyl, (hetero)aryl, heterocyclic, OH, C(O)-R8 or (CHR)rR11;

X = O or S;

p, r = 0-3;

q = 0-2;

R8 = OH, (hetero)aryl, alkoxy, (cyclo)alkyl or heterocyclic;

R9, R10 = H, (amino)alkyl, (hetero)aryl, cycloalkyl or heterocyclic; or

NR9R10 = ring with C, N, O or S;

R11 = OH, NH2, mono/di-substituted amino, (hetero)aryl, alkoxy, (cyclo)alkyl or heterocyclic;

R12 = (hetero)aryl, alkoxy, (cyclo)alkyl or heterocyclic;

Z = OH, O-alkyl or NR3R4;

R3, R4 = H, (hetero)aryl, (cyclo)alkyl or heterocyclic; or

NR3R4 = ring with CH2, N, O or S, or group of formula (i);

Y = CH2, O, N or S; or

Q = C or N;

n = 0-4; and

m = 0-3.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Tyrosine kinase inhibitor; Topoisomerase inhibitor; Thymidylate synthase inhibitor; Irreversible steroidal aromatase inactivator; Pyrimidine antagonist; Purine antagonist; Ribonucleotide reductase inhibitor.

USE - (I) is useful in the treatment of cancers (particularly colon cancer and non-small cell lung cancer) (claimed).

ADVANTAGE - The combination of (I) and (A) are administered at a dose lower than the current standard, providing beneficial efficacy and enhanced effect in the treatment of cancer and reducing the toxicity of (A). The enhanced anti-tumor efficacy of compounds (I) in combination with docetaxel was determined using MX-1 human breast carcinoma subcutaneous tumor model with (I) alone as control. The results showed that combined treatment with (I) and docetaxel resulted in a percentage inhibition value of 82 (53 for control).

Dwg.0/8

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-B03; B02-Z; B04-A07A; B04-B03A; B04-G01; B04-G21; B04-M01; B05-A03B; B05-B01J; B06-D01; B06-H; B07-H; B10-A09B; B10-A13D; B10-B01A; B10-B02A; B14-D03; **B14-H01**; B14-L06; **B14-S09**

TECH UPTX: 20040629

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The salt of (I) is a malate salt. (A) are taxanes, vinca alkaloids, topoisomerase I inhibitors or topoisomerase II inhibitors (preferably paclitaxel, docetaxel (taxotere), vinblastine, vincristine, vindesine, irinotecan, doxorubicin, epirubicin, leucovorin, etoposide, teniposide, idarubicin, gemcitabine, daunorubicin, carboplatin, cisplatin, oxaliplatin, chlorambucil, melphalan, cyclophosphamide, ifosfamide, temozolomide, thiotepa, mitomycin C, busulfan, carmustine, lomustine, 5-fluorouracil,

capecitabine, exemestane, methotrexate, trimetrexate, fluorouracil, fluorodeoxyuridine, azacytidine, mercaptopurine, thioguanine, pentostatin, cytarabine, fludarabine, hydroxyurea, bevacizumab, cetuximab, gefitinib and **imatinib**). For the treatment of non-small cell lung cancer, (I) is administered with carboplatin and paclitaxel, or with carboplatin, docetaxel, cisplatin, gemcitabine, 5-fluorouracil, irinotecan or leucovorin. For the treatment of colon cancer, (I) is administered with 5-fluorouracil, oxaliplatin or leucovorin.

ABEX UPTX: 20040629

SPECIFIC COMPOUNDS - The use of 9 compounds (I) are specifically claimed, i.e. 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-morpholin-4-yl-ethyl)-amide, (S)-5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, (R)-5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, 5-(5-chloro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-ethylamino-ethyl)-amide and 3-(3,5-dimethyl-4-(4-morpholin-4-yl-piperidine-1-carbonyl)-1H-pyrrol-2-methylene)-5-fluoro-1,3-dihydro-indol-2-one.

ADMINISTRATION - Administration of (I) is 25-1500 (preferably 3 mg/m2/day), orally or parenterally.

DEFINITIONS - Preferred Definitions:
R1 = halo (preferably F or Cl);
Z = NR3R4 or group of formula (i);
R3, R4 = lower alkyl or preferably a morpholine ring;
Y = CH2;
R2 = methyl (bonded at 3 and 5 positions);
m = 0;
n, q = 2; and
p = 1.

L89 ANSWER 51 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-365099 [34] WPIX
DOC. NO. CPI: C2004-137846
TITLE: Pharmaceutical composition, useful for the treatment, prevention and management of a myelodysplastic syndrome, comprises an immunomodulatory compound and optionally a carrier and a second active ingredient.
DERWENT CLASS: B02
INVENTOR(S): ZELDIS, J B
PATENT ASSIGNEE(S): (CELG-N) CELGENE CORP; (ZELD-I) ZELDIS J B
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004035064	A1	20040429	(200434)*	EN	47	A61K031-724

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM
ZW

AU 2003228508	A1 20040504	(200467)		A61K031-724
US 2004220144	A1 20041104	(200473)		A61K038-19
EP 1487461	A1 20041222	(200501)	EN	A61K031-724

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004035064	A1	WO 2003-US11323	20030413
AU 2003228508	A1	AU 2003-228508	20030413
US 2004220144	A1 Provisional	US 2002-418468P	20021015
		US 2003-411649	20030411
EP 1487461	A1	EP 2003-726262	20030413
		WO 2003-US11323	20030413

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003228508	A1 Based on	WO 2004035064
EP 1487461	A1 Based on	WO 2004035064

PRIORITY APPLN. INFO: US 2002-418468P 20021015; US 2003-411649 20030411

INT. PATENT CLASSIF.:
MAIN: A61K031-724; A61K038-19
SECONDARY: A61K031-496; A61K031-7056

BASIC ABSTRACT:

WO2004035064 A UPAB: 20040527

NOVELTY - A pharmaceutical composition comprises an immunomodulatory compound or its salt, solvate, hydrate, stereoisomer, clathrate or prodrug and optionally a carrier and a second active ingredient.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) A method of reducing or avoiding an adverse effect associated with the administration of a second active ingredient in a patient suffering from a myelodysplastic syndrome involving administering the second active ingredient and the immunomodulatory compound;

(2) A single dosage unit form comprising the immunomodulatory compound and the second active ingredient;

(3) A kit comprising a composition containing the immunomodulatory compound and umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow and optionally the second active ingredient; and

(4) Treating, preventing and managing a myelodysplastic syndrome involving determining if the patient has a De15q31-33 abnormality and administering the immunomodulatory compound.

ACTIVITY - Antianemic; Neuroprotective; Cytostatic; Immunosuppressive.

MECHANISM OF ACTION - Cytokine production modulator.

An in vitro study was carried out to investigate the effect of 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione (Ia) on the inhibition of TNF- alpha production following LPS-stimulation of human PBMC according to the methods described by Muller et al.,

Bioorg.Med.Chem.Lett.9:1625-1630, 1999) The test compound showed an IC50 value of 25.9 ng/ml.

USE - The composition is useful for the treatment, prevention and management of primary or secondary myelodysplastic syndrome in patients having a De15q31-33 abnormality. The myelodysplastic syndrome includes refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation and chronic myelomonocytic leukemia (Claimed). The composition is also useful in combination with transplantation therapy to reduce the risk of graft versus host disease.

ADVANTAGE - The components of the composition show synergism

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-B02; B02-Z; B03-A; B04-G21; B04-H04A; B04-H04C; B04-H08; B04-N06; B06-D02; B06-D03; B06-D09; B06-D18; B06-E05; B07-A02A; B07-D04C; B07-D11; B07-D12; B10-A15; B10-C04C; B14-F03; B14-G02; B14-G03; **B14-H01A**; B14-N16; **B14-S09**

TECH UPTX: 20040527

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compound: The immunomodulatory compound is of formula (I) or (II).

X and Y = CO or CH2;
R2 = H or lower alkyl;
R1 = H, 1-8C alkyl, 3-7C cycloalkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl, 0-4C alkyl-(1-6C)heterocycloalkyl, 0-4C alkyl-2-5C heteroaryl, C(O)R3, C(S)R3, C(O)OR4, 1-8C alkyl-N(R6)2, 1-8C alkyl-OR5, 1-8C alkyl-C(O)OR5, C(O)NHR3, C(S)NHR3, C(O)NR3R3', C(S)NR3R3' or 1-8C alkyl-O(CO)R5;
R2' = H, F, benzyl, 1-8C alkyl, 2-8C alkenyl or 2-8C alkynyl;
R3 and R3' = 1-8C alkyl, 3-7C cycloalkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl, 0-4C alkyl-(1-6C)heterocycloalkyl, 0-4C alkyl-(2-5C)heteroaryl, 0-8C alkyl-N(R6)2, 1-8C alkyl-OR5, 1-8C alkyl-C(O)OR5, 1-8C alkyl-O(CO)R5 or C(O)OR5;
R4 = 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl, 1-4C alkyl-OR5, benzyl, aryl, 0-4C alkyl-1-6C heterocycloalkyl or 0-4C alkyl-2-5C heteroaryl;
R5 = 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl or 2-5C heteroaryl;
R6 = H, 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl, 2-5C heteroaryl or 0-8C alkyl-C(O)OR5;
R6+R6 = heterocycloalkyl;
n = 0 or 1;
a = chiral-carbon center.
Provided that one of X and Y is CO and the other of X and Y is CO or CH2.
The immunomodulatory compound is selected from:
(1) a cyano or carboxy derivative of a substituted styrene;
(2) a 1-Oxo-2-(2,6-dioxo-3-fluoropiperidin-3-yl)isoindoline derivative;
(3) a 1,3-dioxo-2-(2,6-dioxo-3-fluoropiperidine-3-yl)isoindoline derivative; and
(4) a tetra-substituted 2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindoline derivative.
Preferred components: The second active ingredient improves blood cell production and is selected from:
(1) cytokine;
(2) hematopoietic growth factor;
(3) anti-cancer agent;
(4) antibiotic;
(5) proteasome inhibitor;
(6) immunosuppressive agent (preferably etanercept, **imatinib**,

anti-TNF-alpha antibody, infliximab, G-CSF, GM-CSF, EPO, topotecan, pentoxifyline, ciprofloxacin, irinotecan, vinblastine, dexamethasone, interleukin(IL)-2, IL-8, IL-18, ara-C, vinorelbine, isotretinoin, 13-cis-retinoic acid or their active mutant or derivative).
Preferred Kit: The kit additionally comprises a device for the administration of the composition or the single unit dosage form.

ABEX UPTX: 20040527

SPECIFIC COMPOUNDS - The use of 4-(amino)-2-(2,6-dioxo(3-piperidyl)-isoindoline-1,3-dione; and 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione (Ia) is specifically claimed as the immunomodulatory compounds.

ADMINISTRATION - The immunomodulatory compound is administered during or after transplanting umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in a patient.
The single dosage unit form is administered intravenously or subcutaneously (all claimed). The composition is administered orally, mucosally (e.g. nasally, sublingually, vaginally, buccally or rectally) or parenterally (e.g. subcutaneously, intravenously, through bolus injection, intramuscularly or intraarterially), transdermally or transcutaneously.
The immunomodulatory compound is administered in a dosage of 0.10 - 150 mg or 0.1, 1, 2, 5, 7.5, 10, 12.5, 15, 17.5, 20, 25, 50, 100, 150 or 200 mg.
The second active ingredient is administered intravenously or subcutaneously in a dosage of 1 - 1000 (preferably 5 - 500, especially 10 - 350, particularly 50 - 200) mg.

L89 ANSWER 52 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-340814 [31] WPIX
DOC. NO. CPI: C2004-129432
TITLE: Use of 4-(4-methylpiperazin-1-ylmethyl)-N-(4-methyl-3-(4-pyridin-3-ylpyrimidin-2-ylamino)phenyl)benzamide in the manufacture of medicament for treatment of cancer expressing breast cancer resistance protein.
DERWENT CLASS: B03
INVENTOR(S): HOUGHTON, P J; TRAXLER, P
PATENT ASSIGNEE(S): (NOVS) NOVARTIS AG; (NOVS) NOVARTIS PHARMA GMBH; (SJUD-N) ST JUDE CHILDREN'S RES HOSPITAL
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004032925	A1	20040422	(200431)*	EN	19	A61K031-44
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LT LU LV MA MD MK MN MX NI NO NZ OM PG PH PL PT RO RU SC SE SG SK SY TJ TM TN TR TT UA US UZ VC VN YU ZA ZW						
AU 2003273986	A1	20040504	(200465)			A61K031-44

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004032925	A1	WO 2003-EP11271	20031010
AU 2003273986	A1	AU 2003-273986	20031010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003273986	A1 Based on	WO 2004032925

PRIORITY APPLN. INFO: US 2002-417915P 20021011
INT. PATENT CLASSIF.:
MAIN: A61K031-44
SECONDARY: A61K031-137; A61K031-335; A61K031-4745; A61K031-704; **A61P035-00**

BASIC ABSTRACT:

WO2004032925 A UPAB: 20040514

NOVELTY - In the manufacture of medicament for the treatment of cancer expressing breast cancer resistance protein (BCRP), 4-(4-methylpiperazin-1-ylmethyl)-N-(4-methyl-3-(4-pyridin-3-ylpyrimidin-2-ylamino)phenyl)benzamide (**imatinib**) or its salts are used.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for treatment of the cancer that expresses BCRP, involving administration of an anticancer agent and **imatinib** or its salts.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Breast cancer resistance protein inhibitor; Topoisomerase I Inhibitor.

Human osteosarcoma cells were incubated with topotecan alone for control and a combination of topotecan and **imatinib** (1 micro M) for test. The results indicated that the IC50 value for test/control was 35/254 nM respectively.

USE - In manufacture of medicament for treatment of cancer expressing and over expressing BCRP; inhibiting BCRP; improving the absorption of orally administered anticancer agent by inhibiting BCRP in a patient having cancer (e.g. colon cancer, breast cancer, liver cancer, ovarian cancer, fibrosarcoma, myeloma, acute myeloid leukemia (AML), gastric cancer or non-small cell lung cancer) (claimed).

ADVANTAGE - **Imatinib** improves the absorption of an orally administered anticancer agent and prevents or reverses resistance to it. Also it inhibits breast cancer resistance protein.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B02-D; B02-T; B04-C02; B04-C03C; B05-B01B; B06-E05; B07-D04C; B07-D11; B07-D12; B08-D02; B14-D09; **B14-H01**; B14-L06; **B14-S09**

TECH UPTX: 20040514

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The anticancer agent is anthracycline cytotoxic agent or campothecin-derived topoisomerase I inhibitor (preferably mitoxanthrone, doxorubicin, topotecan, irinotecan, 7-ethyl-10-hydroxycamptothecin (SN-38), 9-aminocamptothecin, 9-nitrocamptothecin, lurtotecan, diflomotecan, BAY38-3441, 7-(2-trimethylsilyl)ethylcamptothecin, 10-hydroxy-7-tert-butyldimethylsilylcamptothecin, CT2016, DE310, T-0128 or PROTHECAN (RTM; PEG-campothecin) (especially topotecan, irinotecan, SN-38, mitoxanthrone or doxorubicin)). **Imatinib** is in the form of the mesylate salt.

ABEX UPTX: 20040514

ADMINISTRATION - The administration is oral (claimed). The dosage is 100 - 1000 (preferably 400 - 600) mg/day.

EXAMPLE - No relevant example given.

L89 ANSWER 53 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-315711 [29] WPIX
DOC. NO. CPI: C2004-119711

TITLE: Composition useful for inducing apoptosis in cancer cells, e.g. chronic myeloid leukemia cells, comprises a tyrosine kinase inhibitor and a histone deacetylase inhibitor.
DERWENT CLASS: B05
INVENTOR(S): BHALLA, K N; NIMMANAPALLI, R
PATENT ASSIGNEE(S): (UYSF-N) UNIV SOUTH FLORIDA
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004026234	A2	20040401	(200429)*	EN	12	A61K000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW						
US 2004127571	A1	20040701	(200444)			A61K031-19
AU 2003270668	A1	20040408	(200462)			A61K000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004026234	A2	WO 2003-US28964	20030919
US 2004127571	A1 Provisional	US 2002-319563P	20020919
		US 2003-605283	20030919
AU 2003270668	A1	AU 2003-270668	20030919

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003270668	A1 Based on	WO 2004026234

PRIORITY APPLN. INFO: US 2003-605283 20030919; US 2002-319563P 20020919
INT. PATENT CLASSIF.:
MAIN: A61K000-00; A61K031-19
BASIC ABSTRACT:
WO2004026234 A UPAB: 20040505
NOVELTY - A composition for inducing apoptosis in cancer cells comprises a tyrosine kinase inhibitor and a histone deacetylase inhibitor.
ACTIVITY - Cytostatic.
MECHANISM OF ACTION - Apoptosis inducer; Tyrosine kinase inhibitor; Histone deacetylase inhibitor.
The effect of tyrosine kinase inhibitor, e.g. **imatinib** mesylate (a), alone and in combination with histone deacetylase inhibitor, e.g. suberoylanilide hydroxamic acid (b), was determined in Lama-84 cells. The cells were exposed for 48 days and the % apoptosis was determined. The results showed that the combination of (a) and (b) was effective on an exposure-dependent basis and induced more apoptosis of the cells compared to the treatment with (a) or (b) alone.
USE - For inducing apoptosis in cancer cells (such as leukemia cells and **imatinib** mesylate refractory cells); and for potentiating a cytotoxic effect of a tyrosine kinase inhibitor by contacting target cells with a histone deacetylase inhibitor (claimed), in the treatment of e.g.

accelerated and blast phases of chronic myeloid leukemia and Bcr-Abl positive acute lymphoblastic leukemia.

ADVANTAGE - The tyrosine kinase inhibitor inhibits binding of ATP with Bcr-Abl protein; preventing the Bcr-Abl protein from carrying out its kinase activity for apoptosis inhibition. The histone deacetylase inhibitor induces apoptosis by causing hyper-acetylation of the amino terminal lysine residues of core nucleosomal histones and of specific transcriptional regulators. The histone deacetylase inhibitor also downregulates levels and autophosphorylation (the addition of phosphate group) of Bcr-Abl, resulting in enhanced apoptosis of target cells when combined with the Bcr-Abl receptor tyrosine kinase inhibitor, compared to the treatment with either agent alone.

Dwg.0/3

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B07-D04C; B07-D11; B07-D12; B10-A18; B14-D06; B14-D07; **B14-H01**; **B14-H03**; **B14-S09**

ABEX UPTX: 20040505

SPECIFIC COMPOUNDS - **Imatinib** mesylate is specifically claimed as the tyrosine kinase inhibitor.
Suberoylanilide hydroxamic acid is specifically claimed as the histone deacetylase inhibitor.

ADMINISTRATION - The administration is for 48 hours (claimed). No dosage given.

EXAMPLE - No relevant example given.

L89 ANSWER 54 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-558867 [52] WPIX
DOC. NO. NON-CPI: N2003-444359
DOC. NO. CPI: C2003-150507
TITLE: Identifying enzyme for designing anti-cancer compound, by selecting enzyme from genes and/or proteins whose expression level is more than two-fold in tumor tissue, as compared to normal cells or tissue.
DERWENT CLASS: B02 B03 B04 D16 S03
INVENTOR(S): ISHITSUKA, H; OKABE, H; SHIMMA, N; TSUKUDA, T; UMEDA, I
PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (CHUS) CHUGAI SEIYAKU KK; (ISHI-I) ISHITSUKA H; (OKAB-I) OKABE H; (SHIM-I) SHIMMA N; (TSUK-I) TSUKUDA T; (UMED-I) UMEDA I
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003043631	A2	20030530	(200352)*	EN	118	A61K031-337
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW						
US 2003138864	A1	20030724	(200352)			G01N033-574
AU 2002352048	A1	20030610	(200419)			A61K031-337
EP 1492523	A2	20050105	(200504)	EN		A61K031-337
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						
BR 2002014386	A	20041130	(200506)			A61K031-337

NO 2004002609 A 20040622 (200513) A61K031-337

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003043631	A2	WO 2002-EP12911	20021118
US 2003138864	A1	US 2002-301460	20021121
AU 2002352048	A1	AU 2002-352048	20021118
EP 1492523	A2	EP 2002-787721	20021118
		WO 2002-EP12911	20021118
BR 2002014386	A	BR 2002-14386	20021118
		WO 2002-EP12911	20021118
NO 2004002609	A	WO 2002-EP12911	20021118
		NO 2004-2609	20040622

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002352048	A1 Based on	WO 2003043631
EP 1492523	A2 Based on	WO 2003043631
BR 2002014386	A Based on	WO 2003043631

PRIORITY APPLN. INFO: EP 2002-5298 20020312; EP 2001-127401 20011123; EP 2001-130245 20011219

INT. PATENT CLASSIF.:
MAIN: A61K031-337; G01N033-574
SECONDARY: A61K031-401; A61K031-4011; A61K031-426; A61K031-4266; A61K031-4725; A61K031-47255; A61K031-4745; A61K031-47455; A61K031-506; A61K031-5066; A61K031-513; A61K031-517; A61K031-5177; A61K031-53; A61K031-533; A61K031-704; A61K031-7044; A61K031-7068; A61K031-70688; A61K031-7072; A61K031-7076; A61K031-70766; C07D305-14; C07D405-02; C07D498-14; C07H019-48; C12Q001-68; C12Q001-688; G01N033-50; G01N033-500

BASIC ABSTRACT:

WO2003043631 A UPAB: 20030813

NOVELTY - Identifying (M1) an enzyme for designing an anti-cancer compound selectively converted to active substances in tumors, involves comparing the expression levels of genes and/or proteins in human tissue and/or cells from normal and tumor origin, and selecting an enzyme of which mRNA and/or protein levels in tumor tissue are higher by more than two-fold as compared to normal cells or tissue.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) use of enzyme identified by M1 for obtaining, identifying and/or designing anti-cancer compounds that can be converted to active substances selectively in tumors;

(2) identifying (M2) anti-cancer compounds that can be converted to active substances selectively in tumors, by generating cells expressing an enzyme of which protein levels in tumor tissue are higher by more than two-fold as compared to normal cells or tissue, and determining growth inhibitory activities of the anti-cancer compounds;

(3) anti-cancer prodrugs of formula X-Y-Q (I) or its salts;

(4) preparation of (I), where a compound Q-Y-H is condensed with a reactive derivative of X; and

(5) a pharmaceutical composition (PC) comprising (I).

X = pro-moiety that is designed to generate an active anti-cancer substance (Q-Y-H) selectively in tumors by the enzymes identified by M1;

Q = a radical derived from the active anti-cancer substance (Q-Y-H); and

Y = -O-, -S- or -N-.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - Farnesyltransferase-Inhibitor; EGF-Receptor-**Tyrosine-Kinase** Inhibitor (claimed). No biological data is given.

USE - M1 is useful for identifying an enzyme (such as microsomal dipeptidase, arylsulfatase A, pyrroline 5'-carboxyreductase, dehydrodiol dehydrogenase, carbonylreductase, lysyl hydroxylase, prolidase, dihydropyrimidinase, glutamine:fructose-6-phosphate amidotransferase, UDP-galactose ceramide galactosyl transferase, lysyl oxidase, enolase, glucose-6-phosphate dehydrogenase, steroyl-coenzyme A desaturase, epoxide hydrolase or aldolase C) for designing an anti-cancer compound that is selectively converted to active substances in tumors. (I) is useful for preparing medicaments for the treatment of cell proliferative disorders such as cancer, preferably colorectal, lung, breast, stomach, cervical or bladder cancer, or solid tumor, or in therapy. (I) is also useful for treating cell proliferative disorders (all claimed).

Dwg.0/0

FILE SEGMENT: CPI EPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B02-D; B04-B03A; B04-L01; B06-H; B07-D03; B07-F01; B11-C07A4; B11-C08E3; B12-K04A1; B12-K04F; B14-D06; B14-H01; D05-H08; D05-H09; D05-H12A; D05-H12B; D05-H13
EPI: S03-E14H5

TECH UPTX: 20030813

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The enzyme is identified by analyses of DNA microarray, PCR, Northern blotting and in situ hybridization, differential displays, RNase protection assay, protein arrays, Western blotting, two dimensional gel electrophoresis or enzyme-linked immunosorbent assay, preferably by analyses of DNA microarray or PCR. The normal cells or tissue are from hematopoietic progenitors derived from the bone marrow or umbilical cord blood, intestine, or skin. The human tissue and/or cells from tumor origin is from brain, lung, esophagus, breast, stomach, pancreas, liver, colon, rectum, kidney, ovary, uterus, bladder, prostate, skin and blood.

Preferred Compound: (I) is of formula (II), (III), (IV) or (V).

R0 = a side chain of natural or non-natural amino acid, preferably methyl, benzyl or 2-methylpropyl, cyclohexylmethyl, 2-naphtylmethyl, 4-phenylbenzyl, (4-cyclohexylcyclohexyl)methyl, alkylthiomethyl, cyclohexylthiomethyl or 4-alkoxybenzyl;

Z = 1-3C alkylene or -O-CH(R3)-;

R1 = H or methyl;

R2 = H, branched 3-10C alkyl or 3-8C cycloalkyl;

R3 = H or straight 1-4C alkyl;

Q- = a radical derived from the active anti-cancer substance (Q-Y-H) such as a taxane (such as taxol or taxotere), camptothecin (such as camptothecin or topotecan), anti-cancer nucleoside (such as decitabine or **troxacitabine**), dolastatin (such as dolastatin 10 or dolastatin 14), anthracycline (such as adriamycin or daunomycin), farnesyltransferase inhibitor (such as R-115777 of the formula 6-(1-amino-1-(4-chlorophenyl)-1-(1-methylimidazol-5-yl)methyl)-4-(3-chlorophenyl)-1-methylquinolin-2(1H)-one) or epidermal growth factor (EGF) receptor **tyrosine kinase** inhibitor (such as ZD 1839 having the formula N-(3-chloro-4-fluorophenyl)-7-methoxy- 6-(3-(4-morpholinyl)propoxy)-4-quinazolinamine);

Y = -O-, -S- or -N-;

R4 = benzoyl or tert-butoxycarbonyl;

R5 = H or acetyl;
R6 = H, fluorine, hydroxyl or cyano; and
R7 = H, fluorine or hydroxy; or
R6, R7 = methylidene or fluoromethylidene;
R8 = H or ethynyl;
R9 = H, fluorine, vinyl or ethynyl;
R10 = H or hydroxy;
m = 2 or 3;
p = 1 to 3;
n = 0 to 1;
R11 = H or fluorine;
R12 = H, fluorine, methyl or hydroxy;
R13 = H, amino, nitro or (dimethylamino)methyl;
R14 = H, 1-4C alkyl, (4-methylpiperazinyl)methyl or (tert-butoxyimino)methyl; and
R11, R12, R13, R14 = 5 or 6 membered ring which optionally contains 1 or 2 hetero atom(s) (optionally substituted with 1 to 3 substituent(s) selected from 1-8C alkyl, amino, 1-8C alkylamino and/or di-(1-4C)alkylamino).

ABEX UPTX: 20030813

SPECIFIC COMPOUNDS - 3 compounds are specifically claimed as the taxol or taxotere (III), e.g. 13-((2R,3S)-2-((5S)-(5-((2S)-2-amino-4-methyl-pentanoylamino)-5-hydroxycarbonyl)pentanoyloxy)-3-benzoylamino-3-phenylpropionyloxy)-2alpha-benzyloxy-4alpha,10beta-diacetoxy-1beta,7beta-dihydroxy-5beta,20-epoxy-tax-11-en-9-one (IIIa). 18 compounds are specifically claimed as the anticancer nucleoside (IV), e.g. (2R)-((2S)-amino-3-cyclohexyl-propionylamino)-(3S)-(1-((4S)-hydroxy-(5R)-hydroxymethyl-3-methylene-tetrahydro-furan-(2R)-yl)- 2-oxo-1,2-dihydro-pyrimidine-4-yl-carbamoyloxy)-butyric acid (IVa). 53 compounds are specifically claimed as the camptothecin or its derivative (V), e.g. 20-O-((S)-tryptophyl-gamma-(S)-glutamyl)-20-(S)-camptothecin (Va).

ADMINISTRATION - The composition is administered by oral or parenteral route (claimed) at a dose of 5-500 mg/m2. The composition can also administered by rectal route.

EXAMPLE - Selection of the enzymes that are expressed preferably in tumors but not in granulocyte progenitors and liver was as follows. CD-positive mononuclear cells derived from the human umbilical cord blood and bone marrow were obtained and were cultured on a confluent monolayer of MS5 mouse stromal cell lines in alpha modified Eagle medium (MEM) medium supplemented with 10% (v/v) horse serum (HS), 10% (v/v) fetal bovine serum (FBS), Flt3 ligand (50 ng/ml), SCF (100 ng/ml), and TPO (50 ng/ml), at 37 degreesC under 5% CO2 in humidified air. Floating hematopoietic cells were collected and stained by monoclonal antibodies against PerCP-anti-CD34, PE-anti-CD13 and fluorescein isothiocyanate (FITC)-anti-15. 5 microl of each antibody was added to a 50 l of cell suspension and incubated at 4 degreesC for 25 minutes. After washing with phosphate buffered saline (PBS) containing 10% (v/v) fetal calf serum (FCS), the expression of CD antigens were detected by using fluorescence activated cell sorting (FACS)Calibur. FACS analysis revealed that more than 90% of mononuclear cells prexpressed CD34 progenitor marker after they were expanded in the above condition. When these CD34-positive cells were treated with 50 ng/ml of granulocyte-colony stimulating factor (G-CSF), more than 80% of the cells were differentiated into CD34-negative, CD13- and CD15-positive myeloblasts and myelocytes within 7 days and further into neutrophils within 14 days after addition of G-CSF. DNA chip experiments yielded several hundreds cDNAs of which mRNA was considered to be absent or expressed only at very low levels. In granulocyte progenitors and liver, but was expressed at certain levels in tumors of breast, liver, gastric, colorectum, pancreas, or ovary in more than 50% of the patients. Among

such cDNAs, more than 150 cDNAs that encoded proteins possessing a known catalytic activity were selected. Those enzymes include phospholipase C, microsomal dipeptidase, arylsulfatase A, DT-diaphorase, pyrroline 5'-carboxyreductase, dehydrodiol dehydrogenase, carbonylreductase, lysyl hydroxylase, prolidase, dihydropyrimidinase, gamma-glutamyl transpeptidase, glutamine:fructose-6-phosphate amidotransferase, UDP-galactose ceramide galactosyl transferase, lysyl oxidase, enolase, glucose-6-phosphate dehydrogenase, uridine phosphorylase, steroyl-coenzyme desaturase, epoxide hydrolase, aldolase C.

DEFINITIONS - Preferred Definition:
Q = a taxane (such as taxol or taxotere), camptothecin (such as camptothecin or topotecan), anti-cancer nucleoside (such as decitabine or **troxacitabine**), dolastatin (such as dolastatin 10 or dolastatin 14), anthracycline (such as adriamycin or daunomycin), farnesyltransferase inhibitor (such as R-115777 of the formula 6-(1-amino-1-(4-chlorophenyl)-1-(1-methylimidazol-5-yl) methyl)-4-(3-chlorophenyl)-1-methylquinolin-2(1H)-one) or epidermal growth factor (EGF) receptor **tyrosine kinase** inhibitor (such as ZD 1839 having the formula N-(3-chloro-4-fluorophenyl)-7-methoxy- 6-(3-(4-morpholinyl)propoxy)-4-quinazolinamine).

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:31:38 ON 16 MAR 2005

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 11, 2005 (20050311/UP).

=>

```
=> fil hcap
FILE 'HCAPLUS' ENTERED AT 13:31:51 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 16 Mar 2005  VOL 142 ISS 12
FILE LAST UPDATED: 15 Mar 2005  (20050315/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> fil medlin
FILE 'MEDLINE' ENTERED AT 13:31:56 ON 16 MAR 2005

 FILE LAST UPDATED: 15 MAR 2005 (20050315/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available.  For details enter HELP
 RLOAD at an arrow promt (=>).  See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> fil biosis
FILE 'BIOSIS' ENTERED AT 13:31:58 ON 16 MAR 2005
Copyright (c) 2005 The Thomson Corporation

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 9 March 2005 (20050309/ED)

FILE RELOADED: 19 October 2003.

=> fil embas
FILE 'EMBASE' ENTERED AT 13:32:01 ON 16 MAR 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.
```

FILE COVERS 1974 TO 10 Mar 2005 (20050310/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil drugu
FILE 'DRUGU' ENTERED AT 13:32:07 ON 16 MAR 2005

FILE LAST UPDATED: 10 MAR 2005 <20050310/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

>>> A RECENT REVIEW OF PSYCHIATRIC DISEASE KEYWORDS USED IN DERWENT DRUG FILE HAS PROMPTED A REVISION BASED ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH EDITION).
FOR FURTHER DETAILS:
http://thomsonderwent.com/derwenthome/support/userguides/lit_guide

=> fil wpix
FILE 'WPIX' ENTERED AT 13:32:11 ON 16 MAR 2005

FILE LAST UPDATED: 11 MAR 2005 <20050311/UP>
MOST RECENT DERWENT UPDATE: 200517 <200517/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-revision/
FOR DETAILS. <<<

=> fil pascal
FILE 'PASCAL' ENTERED AT 13:32:17 ON 16 MAR 2005

FILE LAST UPDATED: 14 MAR 2005 <20050314/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
IN THE BASIC INDEX (/BI) FIELD <<<

=> fil jicst
FILE 'JICST-EPLUS' ENTERED AT 13:32:21 ON 16 MAR 2005
COPYRIGHT (C) 2005 Japan Science and Technology Agency (JST)

FILE COVERS 1985 TO 14 MAR 2005 (20050314/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

=> fil conf
FILE 'CONF' ENTERED AT 13:32:24 ON 16 MAR 2005
COPYRIGHT (c) 2005 FIZ Karlsruhe

FILE LAST UPDATED: 11 MAR 2005 <20050311/UP>
FILE COVERS 1976 TO DATE.

=> fil confsci
FILE 'CONFSCI' ENTERED AT 13:32:27 ON 16 MAR 2005
COPYRIGHT (C) 2005 Cambridge Scientific Abstracts (CSA)

FILE COVERS 1973 TO 20 Jan 2005 (20050120/ED)

=> fil mediconf
FILE 'MEDICONF' ENTERED AT 13:32:32 ON 16 MAR 2005
COPYRIGHT (c) 2005 FAIRBASE Datenbank GmbH, Hannover, Germany

FILE LAST UPDATED: 15 NOV 2004 <20041115/UP>
>>> MEDICONF IS NO LONGER BEING UPDATED AS OF 2005 <<<

=> fil scisearch
FILE 'SCISEARCH' ENTERED AT 13:32:36 ON 16 MAR 2005
Copyright (c) 2005 The Thomson Corporation

FILE COVERS 1974 TO 10 Mar 2005 (20050310/ED)

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:32:38 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 11, 2005 (20050311/UP).

=> d his l88

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, DRUGU, WPIX, PASCAL, JICST-EPLUS, CONF, CONFSCI, MEDICONF, SCISEARCH' ENTERED AT 13:14:47 ON 16 MAR 2005)
L88 13 S L87 AND (L14 OR L63 OR L41 OR L12)

```
=> d que l88
L12             QUE  ABB=ON  PLU=ON  STI(1W)571
L14             QUE  ABB=ON  PLU=ON  ?TYROSIN?(2A)?KINAS?
L41             QUE  ABB=ON  PLU=ON  ?IMATINIB?
L62             QUE  ABB=ON  PLU=ON  (?TROXACITABIN? OR ?TROXATYL? OR (SP
                D(1W)758) OR OCCC OR (BCH(1W)(204 OR 4556)) OR (?DIOXALAN
                ?(1W)C))
L63             QUE  ABB=ON  PLU=ON  ((CGP(1W)57148B) OR ?GLEEVAC? OR ?GL
                EEVEC? OR ?GLIVEC?)
L83          2352 SEA GILES, F?/AU
L84           609 SEA VERSTOVSEK, S?/AU
L85           120 SEA (L83 OR L84) AND L62
L86            55 DUP REM L85 (65 DUPLICATES REMOVED)
L87            52 SEA (?CANCER? OR ?CARCIN? OR ?NEOPLAS? OR ?LEUK? OR ?ONCOLO?
                  OR ?PROLIFER? OR ?TUMOR? OR ?TUMOUR?) AND L86
L88            13 SEA L87 AND (L14 OR L63 OR L41 OR L12)
```

=> d ibib ed ab l88 1-
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, DRUGU, WPIX' -
CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L88 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:334928 HCAPLUS
DOCUMENT NUMBER: 140:399534
TITLE: **Troxacitabine** and **imatinib** mesylate combination therapy of chronic myeloid **leukaemia**: preclinical evaluation
AUTHOR(S): Orsolic, Nada; **Giles, Francis J.**; Gourdeau, Henriette; Golemovic, Mirna; Beran, Miloslav; Cortes, Jorge; Freireich, Emil J.; Kantarjian, Hagop; **Verstovsek, Srdan**
CORPORATE SOURCE: Department of Leukemia, M.D. Anderson Cancer Center, The University of Texas, Houston, TX, USA
SOURCE: British Journal of Haematology (2004), 124(6), 727-738
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Apr 2004
AB The in vitro and in vivo activity of a deoxycytidine analog, **troxacitabine**, alone or in combination with **imatinib** mesylate (IM), was evaluated against human chronic myeloid **leukemia** (CML) cell lines both sensitive (KBM5 and KBM7) and resistant (KBM5-R and KBM7-R) to IM. These cell lines differ in their sensitivity to IM but all showed similar sensitivity to treatment with **troxacitabine** (IC50 = 0.5-1 μmol/l). Combined treatment with **troxacitabine** and IM revealed additive or synergistic effects. Greater apoptotic response was seen with, combined treatment than with either agent alone in KBM7-R cells. In clonogenic assays, **troxacitabine** showed activity against mononuclear cells from CML patients (IC50 = 0.01 μmol/l) with either IM-sensitive or resistant disease. In vivo efficacy studies were carried out in severe combined immunodeficient mice bearing KBM5 or KBM5-R cells. **Troxacitabine** was administered i.p. daily for 5 d starting on day 20, at doses of 5, 10, 20, or 25 mg/kg. IM was administered i.p. twice a day for 10 d at a dose of 50 mg/kg starting on day 25. In this setting of late stage disease, **troxacitabine** led to a significant increase in life span, while IM did not. When IM was combined with **troxacitabine** at 10 and 25 mg/kg in the KBM5 xenograft model, a further increase in life span was observed and some mice achieved long-term survival. These data indicate that the combination of **troxacitabine** and IM has significant preclin. activity in advanced CML and that clin. evaluation of this combination is warranted.
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:997599 HCAPLUS
DOCUMENT NUMBER: 140:12393
TITLE: New agents in chronic myelogenous **leukemia**
AUTHOR(S): Cortes, Jorge; **Giles, Francis**
CORPORATE SOURCE: Department of Leukemia, M. D. Anderson Cancer Center, The University of Texas, Houston, TX, USA

SOURCE: Journal of the National Comprehensive Cancer Network (2003), 1(4), 501-512
CODEN: JNCCA4; ISSN: 1540-1405
PUBLISHER: Jones and Bartlett Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 23 Dec 2003
AB A review. Multiple new agents are currently being developed in chronic myelogenous **leukemia** (CML). Most of these agents are now being investigated in patients who have developed resistance to **imatinib**. Their mechanisms of action are diverse and many may be synergistic with **imatinib**. These agents will be used soon in different combinations, most likely including **imatinib**, with the hope of obtaining a complete blockade of the intracellular pathways that are triggered by Bcr-Abl. If this is successful, complete eradication of disease may become a reality for the majority of patients with CML.
REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:621850 HCAPLUS
DOCUMENT NUMBER: 140:228562
TITLE: Phase II study of **troxacitabine**, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib** mesylate-resistant chronic myelogenous **leukemia** in blastic phase
AUTHOR(S): **Giles, Francis J.**; Feldman, Eric J.; Roboz, Gail J.; Larson, Richard A.; Mamus, Steven W.; Cortes, Jorge E.; **Verstovsek, Srdan**; Faderl, Stefan; Talpaz, Moshe; Beran, Miloslav; Albitar, Maher; O'Brien, Susan M.; Kantarjian, Hagop M.
CORPORATE SOURCE: M.D. Anderson Cancer Center, Department of Leukemia, University of Texas, Houston, TX, 77030, USA
SOURCE: Leukemia Research (2003), 27(12), 1091-1096
CODEN: LEREDD; ISSN: 0145-2126
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Aug 2003
AB A phase II study of **troxacitabine**, a non-natural dioxolane nucleoside L-enantiomer, was conducted in patients with chronic myelogenous **leukemia** in blastic phase (CML-BP). Patients were untreated for BP, or treated with **imatinib** mesylate (IM) as sole prior therapy for BP. **Troxacitabine** was given as an i.v. infusion over 30 min daily for 5 days at a dose of 8.0 mg/m2 per day. Thirty-one patients, 29 (93%) of whom had failed prior IM therapy, received 51 courses of therapy. Grade 3 or 4 toxicities included stomatitis (4%), hand-foot syndrome (18%), and skin rash (12%). Four patients (13%) responded. **Troxacitabine**-based combinations merit study in IM-resistant CML.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:356264 HCAPLUS
DOCUMENT NUMBER: 138:348696
TITLE: Pharmaceutical compositions for the treatment of **leukemia** comprising dioxolane nucleosides

analogs
INVENTOR(S): Jolivet, Jacques; **Giles, Francis J.**; Kantarjian, Hagop
PATENT ASSIGNEE(S): Shire Biochem Inc., Can.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037344	A1	20030508	WO 2002-CA1687	20021104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003125305	A1	20030703	US 2002-286960	20021104
US 6645972	B2	20031111		
EP 1441733	A1	20040804	EP 2002-771956	20021104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-330891P P 20011102
WO 2002-CA1687 W 20021104
OTHER SOURCE(S): MARPAT 138:348696
ED Entered STN: 09 May 2003
AB The present invention provides a novel method for treating **leukemia** in a host that has been previously treated with a Bcr-Abl **tyrosine kinase** inhibitor comprising administering to the host a therapeutically effective amount of a dioxolane nucleoside analog.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 5 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2004043980 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14745859
TITLE: New agents in acute myeloid **leukemia** and other myeloid disorders.
AUTHOR: Ravandi Farhad; Kantarjian Hagop; **Giles Francis**; Cortes Jorge
CORPORATE SOURCE: Department of Leukemia, The University of Texas M D Anderson Cancer Center, Houston, Texas 77030, USA.. fravandi@mdanderson.org
SOURCE: Cancer, (2004 Feb 1) 100 (3) 441-54. Ref: 140
Journal code: 0374236. ISSN: 0008-543X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402

ENTRY DATE: Entered STN: 20040128
Last Updated on STN: 20040220
Entered Medline: 20040219

ED Entered STN: 20040128
Last Updated on STN: 20040220
Entered Medline: 20040219

AB Over the past several decades, improvements in chemotherapeutic agents and supportive care have resulted in significant progress in treating patients with acute myeloid **leukemia** (AML). More recently, advances in understanding the biology of AML have resulted in the identification of new therapeutic targets. The success of all-trans-retinoic acid in acute promyelocytic **leukemia** and of **imatinib** mesylate in chronic myeloid **leukemia** have demonstrated that targeted therapy may be more effective and less toxic when well defined targets are available. At the same time, understanding mechanisms of drug resistance and means to overcome them has led to modification of some of the existing cytotoxic agents. Rational design and conduct of clinical trials is necessary to ensure that the full potential of these new agents is realized.

L88 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:152475 BIOSIS
DOCUMENT NUMBER: PREV200200152475
TITLE: Phase II study of **TroxatylTM** in patients with chronic myeloid **leukemia** in blastic phase (CML-BP).
AUTHOR(S): **Giles, Francis** [Reprint author]; Feldman, Eric; Cortes, Jorge [Reprint author]; Faderl, Stefan [Reprint author]; Larson, Richard; Mamus, Steven; Thomas, Deborah [Reprint author]; Garcia-Manero, Guillermo [Reprint author]; O'Brien, Susan [Reprint author]; Beran, Milsolav [Reprint author]; Talpaz, Moshe [Reprint author]; Kantarjian, Hagop [Reprint author]
CORPORATE SOURCE: UT MD Anderson Cancer Center, Houston, TX, USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 258b. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

ED Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

AB **Troxatyl** triphosphate (converted by the intracellular phosphorylation of **Troxatyl**) is a potent inhibitor and chain terminator for human cellular DNA polymerases and was a unique pattern of cellular uptake and metabolism. On a Phase I study, **Troxatyl** had significant **antileukemia** activity in patients with refractory disease. (Giles et al, JCO: 19:762:2001). The recommended single agent dose was defined as 8 mg/m2/day daily for 5 days. On a subsequent Phase II study, 6 patients with CML-BP of 16 evaluable (37%) achieved a return to chronic phase disease. (Giles et al, JCO: In press). Three of the 6 responding patients received **Troxatyl** as first therapy for CML-BP; one patient had failed STI571 as prior sole therapy for CML-BP. A multicenter Phase II study of **Troxatyl** 8

mg/m2/day daily for 5 days for patients with CML-BP who have received no prior chemotherapy for CML-BP is being conducted. Patients who have received **Gleevec** therapy as sole prior therapy for CML-BP are also eligible. Twenty-six patients, 17 male, 26 performance score ltoreq2, median age 54 years (range 31-84) have been entered on study to date, 13 (50%) patients received **Troxatyl** as first therapy for CML-BP, 13 (50%) had failed prior **Gleevec** therapy for CML-BP. Response definitions are as follows: Complete hematologic response (CHR) requires normalization of peripheral counts and differentials with ltoreq5% marrow blasts for at least 4 weeks. Hematologic improvement (HI) is as with CHR but with persistence of thrombocytopenia less than 100X109/L and few immature peripheral cells. A partial hematologic response (PHR) is as per CHR, but allows persistence of, though gtoreq50% reduction of, palpable splenomegaly and thrombocytosis (platelets>450X109/L), or the presence of few immature peripheral cells. Back to second chronic phase (BCP) requires disappearance of BP features and return to chronic phase CML features, i.e., peripheral blasts <15%, peripheral blasts+promyelocytes <30%, peripheral basophils <20%, and platelets >100X109/L. In patients with extramedullary disease (EMD), complete response (CR) requires CHR plus disappearance of all EMD. PR in patients with EMD require at least a 50% reduction in all EMD. Twenty-one patients who have received a total of 40 cycles (range 1 to 4) of **Troxatyl** therapy are currently evaluable for response - 1 PR, 1 HI, 1 BCP, and 1 CR in a patient with EMD have been recorded to date. Four patients died during cycle 1 of therapy - one with a CVA, 3 with sepsis/progressive disease. Extramedullary grade 3 or 4 attributable adverse events in the first cycle of therapy included skin rash (3), hyperbilirubinemia (3), hand foot syndrome (1), colitis (1). One patient developed Sweets Syndrome during 1st cycle of therapy - this subsequently completely resolved. Median survival in the study cohort is 9 months with 33% of patients alive at 1 year. **Troxatyl** has significant activity in patients with CML-BP. Accrual continues on this study.

L88 ANSWER 7 OF 13 EMBASE
on STN

ACCESSION NUMBER: 2004318012 EMBASE
TITLE: Accelerated and blastic phases of chronic myelogenous **leukemia.**
AUTHOR: **Giles F.J.**; Cortes J.E.; Kantarjian H.M.; O'Brien S.M.
CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, The University of Texas, M.D. Anderson Cancer Ctr., 1515 H., Houston, TX, United States. fgiles@mdanderson.org
SOURCE: Hematology/Oncology Clinics of North America, (2004) 18/3 (753-774).
Refs: 177
ISSN: 0889-8588 CODEN: HCNAEQ
PUBLISHER IDENT.: S 0889-8588(04)00010-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Although the mechanisms of CML transformation remain poorly understood, recent therapeutic advances moderately have improved the prognosis of patients in AP and BP. Treatment with IFN-αbased regimens are minimally effective for patients in AP and ineffective for those in BP.

Imatinib mesylate has a significant but generally transient response rate in patients in AP and BP. Hope for progress in this area lies mainly in the development of novel targeted therapies. The more promising agents that are being investigated include decitabine, HHT, **troxacitabine**, clofarabine, farnesyl transferase inhibitors, histone deacetylase inhibitors, and the VEGF and mTOR inhibitors. Many of these approaches may be synergistic with **imatinib** or the more powerful abl or Src inhibitors that are in development.

L88 ANSWER 8 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004165534 EMBASE
TITLE: Novel therapies for patients with chronic myeloid **leukemia.**
AUTHOR: **Giles F.J.**; Kantarjian H.; Cortes J.
CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, University of Texas, MD Anderson Cancer Center, 1400 Holcombe Boulevard, Houston, TX 77030, United States. frankgiles@aol.com
SOURCE: Expert Review of Anticancer Therapy, (2004) 4/2 (271-282). Refs: 177
ISSN: 1473-7140 CODEN: ERATBJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The most immediate issues that will have a major impact on the long-term survival of patients with chronic myeloid **leukemia** is the optimal use of **imatinib** mesylate (**Gleevec.**RTM., Novartis) and the development of effective therapies for those patients who are intolerant of, or become resistant to, optimal doses of this agent. Of the multiple new agents that are currently being developed for patients with chronic myeloid **leukemia**, most are being investigated in patients who have developed resistance to **imatinib** , which is a confounding factor in itself. The mechanisms of action of novel agents are diverse and they may have a variably synergistic therapeutic relationship with **imatinib.** The complete blockade of the intracellular pathways that are triggered by Bcr-Abl, combined with successful reversal of apoptotic and/or angiogenic abnormalities in chronic myeloid **leukemia**, may well lead to a cure for the majority of patients. .COPYRGT. Future Drugs Ltd. All rights reserved.

L88 ANSWER 9 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003396846 EMBASE
TITLE: Phase 2 clinical and pharmacologic study of clofarabine in patients with refractory or relapsed acute **leukemia** .
AUTHOR: Kantarjian H.; Gandhi V.; Cortes J.; **Verstovsek S.** ; Du M.; Garcia-Manero G.; **Giles F.**; Faderl S.; O'Brien S.; Jeha S.; Davis J.; Shaked Z.; Craig A.; Keating M.; Plunkett W.; Freireich E.J.
CORPORATE SOURCE: H. Kantarjian, Department of Leukemia, Box 428, Univ. Texas MD Anderson Cancer Ctr., 1515 Holcombe Blvd, Houston, TX 77030, United States. hkantarj@mdanderson.org
SOURCE: Blood, (1 Oct 2003) 102/7 (2379-2386).

Refs: 40
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In a phase 2 study, 62 patients with relapsed and refractory acute myeloid **leukemia** (AML; n = 31), myelodysplastic syndrome (MDS; n = 8), chronic myeloid **leukemia** in blastic phase (CMLBP; n = 11), and acute lymphocytic **leukemia** (ALL; n = 12) received 40 mg/m(2) clofarabine intravenously over 1 hour daily for 5 days, every 3 to 6 weeks. Twenty patients (32%) achieved complete response (CR), 1 had a partial response (PR), and 9 (15%) achieved CR but without platelet recovery (CRp), for an overall response rate of 48%. In AML, responses were noted in 2 (18%) of 11 patients in first salvage with short first CR (≤ 12 months), in 7 (87%) of 8 patients with longer first CR, and in 8 (67%) of 12 patients in second or subsequent salvage. Responses were observed in 4 of 8 patients with high-risk MDS (50%), in 7 (64%) of 11 with CML-BP, and in 2 (17%) of 12 with ALL. Severe reversible liver dysfunction was noted in 15% to 25%. After the first clofarabine infusion, responders accumulated more clofarabine triphosphate in blasts compared with nonresponders (median 18 vs 10 μM; P = .03). This increased only in responders (median, 1.8-fold; P = .008) after the second clofarabine infusion. In summary, clofarabine is active in acute **leukemias** and MDS; cellular pharmacokinetics may have prognostic significance.

L88 ANSWER 10 OF 13 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-10803 DRUGU P
TITLE: **Troxatyl** and STI571 combination therapy for chronic myeloid **leukemia**: preclinical in vitro and in vivo evaluation.
AUTHOR: Orsolic N; **Giles F**; Beran M; Cortes J; Albitar M; Kantarjian H; **Verstovsek S**
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Blood (100, No. 11, Pt. 1, 786a, 2002) 2 Ref.
CODEN: BLOOAW ISSN: 0006-4971
AVAIL. OF DOC.: Leukemia, The University of Texas, MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The effects of **Troxatyl** (TX, **troxacitabine**) and **imatinib** (IM, **STI-571**) were investigated in-vitro in chronic myeloid **leukemia** (CML) KBM5 and KBM7 cells, IM-resistant sublines KBM5-R and KBM7-R, cells from patients with CML and in-vivo after i.p. administration in mice bearing KBM5 or KBM5-R cells. TX and IM showed a synergistic cytostatic activity both in in-vitro and in-vivo studies. In conclusion, the results show that TX has activity in late stage CML and that combining it with IM is a very reasonable clinical approach. (conference abstract: 44th Annual Meeting of the American Society of Hematology, Philadelphia, Pennsylvania, USA, 2002).

L88 ANSWER 11 OF 13 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-17334 DRUGU T S
TITLE: Phase II study of **Troxatyl** in patients with chronic myeloid **leukemia** in blastic phase (CML-BP).
AUTHOR: **Giles F**; Feldman E; Cortes J; Faderl S; Larson R; Mamus S; Thomas D; Garcia Manero G; O'Brien S; Beran M; Talpaz M; Kantarjian H
CORPORATE SOURCE: Anderson-Cancer-Cent.; Univ.Chicago; Univ.Cornell
LOCATION: Houston, Tex., New York, N.Y., Chicago, Ill.; Orlando, Fla., USA
SOURCE: Blood (98, No. 11, Pt. 2, 258b, 2001) 1 Ref.
CODEN: BLOOAW ISSN: 0006-4971
AVAIL. OF DOC.: UT MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The efficacy of **troxacitabine** (**Troxatyl**) was investigated in 26 patients with chronic myeloid **leukemia** in blastic phase (CML-BP) in a phase II study. Side-effects included skin rash, hyperbilirubinemia, hand foot syndrome, colitis, and Sweets syndrome. The result showed that **Troxatyl** had significant activity in these CML-BP patients. (conference abstract: 43rd Annual Meeting of the American Society of Hematology, Orlando, Florida, USA, 2001).

L88 ANSWER 12 OF 13 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-12589 DRUGU T S
TITLE: **Troxatyl** is effective in non-lymphoid blastic phase chronic myeloid **leukemia** (CML-BP).
AUTHOR: **Giles F**; Talpaz M; Bivins C; Jolivet J; Kantarjian H
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Eur.J.Cancer (37, Suppl. 6, S35, 2001) 2 Ref.
CODEN: EJCAEL ISSN: 0964-1947
AVAIL. OF DOC.: University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The use of **troxacitabine** (**Troxatyl**) to treat 17 patients with non-lymphoid blastic phase chronic myeloid **leukemia** (CML-BP) is reported. Side-effects included rash, hand-foot syndrome and mucositis. Median survival was over 52 wk. **Troxatyl** as a single agent in CML-BP is under study in Phase II trial. (conference abstract: 11th European **Cancer** Conference, Lisbon, Portugal, 2001).

L88 ANSWER 13 OF 13 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-480817 [45] WPIX
DOC. NO. CPI: C2004-178848
TITLE: Combination, useful for the treatment of **leukemia** e.g. acute myelogenous **leukemia** and chronic myelogenous **leukemia**, comprises isoxazole derivatives and a Bcr-Abl **tyrosine kinase** inhibitor.
DERWENT CLASS: B03
INVENTOR(S): **GILES, F J**; **VERSTOVSEK, S**

PATENT ASSIGNEE(S): (GILE-I) GILES F J; (VERS-I) VERSTOVSEK S; (SHIR-N) SHIRE BIOCHEM INC
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004052369	A1	20040624	(200445)*	EN	55
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2004192652	A1	20040930	(200465)		
AU 2003291882	A1	20040630	(200472)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004052369	A1	WO 2003-CA1909	20031208
US 2004192652	A1 Provisional	US 2002-431196P	20021206
		US 2003-729387	20031208
AU 2003291882	A1	AU 2003-291882	20031208

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003291882	A1 Based on	WO 2004052369

PRIORITY APPLN. INFO: US 2002-431196P 20021206; US 2003-729387 20031208
ED 20040716
AB WO2004052369 A UPAB: 20040716
NOVELTY - Pharmaceutical combination (A) comprises isoxazole derivatives (I) and their salts and a Bcr-Abl **tyrosine kinase** inhibitor (B).

DETAILED DESCRIPTION - Pharmaceutical combination (A) comprises isoxazole derivatives of formula (I) and their salts and a Bcr-Abl **tyrosine kinase** inhibitor (B).

B = cytosine or 5-fluorocytosine;

R = H, mono-tri phosphate, carbonyl substituted with 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 6-10C aryl or -P(O)2ORc; and

Rc = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or hydroxy protecting group.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - **Tyrosine kinase** inhibitor.

USE - (A) is useful for the treatment of **leukemia** e.g. acute myelogenous **leukemia**, chronic myelogenous **leukemia** in blastic phase, refractory/relapsed **leukemia** and chronic myelogenous **leukemia.**

ADVANTAGE - (A) has synergistic effect to reduce the **leukemia**.

The effect of (A) in treating **leukemia** was assessed using an in vivo study in mice. The results showed that the combination of **Troxatyl** with **STI-571** provided a synergistic effect in treating **leukemia.**

Dwg.0/14

```
=> file stnguide
FILE 'STNGUIDE' ENTERED AT 13:33:13 ON 16 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 11, 2005 (20050311/UP).

=>
```